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USSR Report

LIFE SCIENCES

EFFECTS OF NONIONIZING ELECTROMAGNETIC RADIATION

No. 6

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CONTENTS

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STIMULATING EFFECT OF EXPOSURE OF RAT STERNUM TO VARIABLE MAGNETIC FIELD ON ANTIBODY PRODUCTION IN THE SPLEEN

Kiev FIZIOLOGICHESKIY ZHURNAL in Russian Vol 28, No 1, Jan-Feb 82 (manuscript received 19 Oct 79) pp 109-112

[Article by O. F. Mel'nikov, A. A. Diyesperova, E. A. Bakay and A. I. Rudoy, Kiev Institute of Otolaryngology]

[Text] An intensive search is currently in progress for agents capable of selectively altering functional activity of the immunogenetic system. This is attributable to the demands of modern infectious immunology, allergology and transplantology. Along with greater use of biological agents, most often from thymus tissue [3, 4, 5, 10, 13] and synthetic analogues thereof, use is also made of physical factors [2, 8]. In particular, it was demonstrated that exposure to variable electromagnetic fields could activate antibody genesis [1]. However, not only the entire system of lymphoid tissue, but other organs and systems are exposed to magnetic fields, which is not always desirable.

We made an experimental study of the possibility of stimulating antibody production by exposing the sternum, at the projection of the thymus, to a variable frequency magnetic field.

Methods

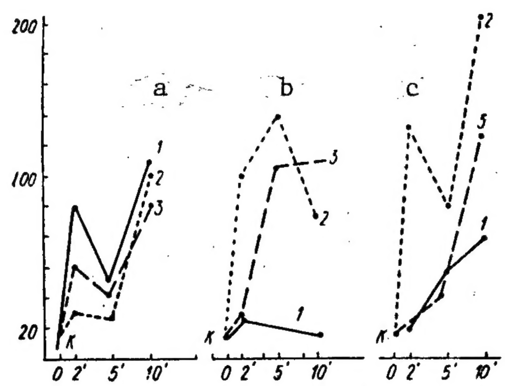
These studies were conducted on 150 albino laboratory rats 5 months of age, weighing 200 g. The working part of the variable magnetic field generator was placed on the chest in the region of projection of the thymus in such a position as to have the sternum and thymus in a quasistationary homogeneous magnetic flux. The generator enabled us to alter the magnetic flux uniformly or in steps in the range of 0 to 0.025 T.

We studied several parameters that could affect the level of the antibody response, and first of all the effect of intensity of the magnetic field, for which purpose we tested fields of 0.005, 0.015 and 0.025 T. Then, at each level of energy, we tested the effect of exposure time (2.5 and 10 min) and time of administration of test antigen--heteroerythrocytes (ram erythrocytes--RE). We used simultaneous immunization, when RE was given on the day of exposure to the magnetic field, subsequent, when RE was given 1 day after exposure, and preliminary, 1 day before exposure to the magnetic field. We evaluated antibody production on the 5th day after intraperitoneal injection of RE, counting the antibody-producing cells (APC) in the spleen according to

[11]. The obtained data were submitted to statistical processing with use of the t test of Student.

Results

The results of studying antibody genesis in the spleen are submitted in the form of mean data on the effect of magnetic fields varying in intensity on the sternum-thymus complex. At 0.005 T (see Figure, a), local exposure of lymphoid organs reliably increased antibody production in the spleen in the case of simultaneous or preliminary RE immunization, even with exposure for 2 min; exposure for 5 min had no effect, whereas 10 min exposure stimulated antibody synthesis by 4-5 times, as compared to the control, with all of the immunization variants ($p<0.01$).



Number of antibody-producing cells (APC) in rat spleen with single exposure of sternum in area of projection of the thymus to variable electromagnetic fields differing in intensity and with different times of administration of antigen

Y-axis, number of APC/10^6 splenocytes; X-axis, exposure time, min. Each point corresponds to the mean obtained in the experiment for 5 animals. The control groups are shown at the starting point (0 on the X-axis)

a) exposure of sternum to 0.005 T variable magnetic field in the region of projection of the thymus
b) 0.015 T
c) 0.025 T
1) RE on day of exposure
2) RE day after exposure
3) RE 1 day before exposure

An increase to 0.015 T was associated with other consequences (see Figure, b). Immunization of animals concurrently with exposure was not associated with appreciable stimulation of antibody production, regardless of exposure time. Subsequent immunization (RE given 1 day after exposure to magnetic field) led to 4-fold increase in antibody production with exposure for 2 min, 10-fold with 5-min exposure and 5-fold with 10-min exposure. Preliminary immunization had a relatively low stimulating effect on antibody production with 2-min exposure and about the same effect (5-6-fold) with 5 and 10 min exposure.

The figure, c, illustrates the results of studying antibody production with the use of a 0.025 T magnetic field. Under these conditions, we obtained the following results. Simultaneous and preliminary immunization had no appreciable effect on antibody genesis with 2-min exposure to the magnetic field. Under these conditions, administration of RE enhanced the immune response reliably only with 5 and 10-min exposure. Subsequent injection of RE stimulated reliably production of primary IgM in the animals' spleen. Thus, there was a 7.5-fold increase in number of APC with exposure for 2 min, 4.2-fold with 5-min exposure and 11-fold with 10-min exposure, as compared to the control.

Discussion

Thus, the results of our studies were indicative of a basically important fact: it is possible to enhance antibody genesis in lymphoid tissue by local use of a variable magnetic field.

We established that local exposure of the sternum and thymus to a magnetic field is associated with intensification of the primary antibody response of the spleen of experimental animals. This stimulation is not the same with use of variable magnetic fields, and depends appreciably on intensity thereof, exposure time and time of administration of antigen.

The studies revealed that the intensification of the antibody response increases with increase in field intensity. Thus, a variable magnetic field of 0.025 T elicited substantially greater activation of antibody genesis than a field of 0.005 T.

Exposure time has a substantial significance, although in this case significant deviations are also observed. Thus, with intensities of 0.005 and 0.025 T, maximum stimulation was produced when exposure lasted 2 and 10 min, whereas in a magnetic field of 0.015 T this was demonstrated with 5 and 10 min exposure. Thus, an increase in exposure time to 10 min was usually associated with a considerable stimulating effect.

The time of administration of test antigen is also very important. At the above intensities and exposure times, stimulation was the most stable when antigen was injected 1 day after exposure to the magnetic field. This effect was less distinct in the case of preliminary and simultaneous immunization Evidently, the initial processes of immunogenesis are believed [2] to be the most sensitive to magnetic fields. The results of our studies could also serve as an indirect confirmation. With the use of low intensity, preliminary and simultaneous immunization had a greater stimulating effect with a given exposure time than with 5-fold increase in intensity.

As for the mechanisms of effects of variable magnetic fields on the immunity system, this question has been virtually unexplored as yet. It can be assumed that there can be appreciable intensification of differentiation of thymus cells and production of thymus humoral factors important to immunogenesis [3, 7, 10] as a result of the effect of the magnetic field on the central organ of immunity, the thymus.

In addition to the above factors, there may also be stimulation of histogenesis and synthesis of various substances in the sternal bone marrow, which is a source of stem cells and humoral factor [6], and this is largely instrumental in strengthening the cellular potential of the lymphoid system and processes of cell cooperation, i.e., ultimately stimulation.

A magnetic field, like other physical factors, is a nonspecific stimulus for cells and tissues, and the reaction to this stimulation is capable of intensifying many processes in an organism, including immunogenesis.

The possibility of stimulating immunity by exposing central immunity organs to a magnetic field opens up propsects, not only with regard to theoretical work in the field of stimulation, but, also, to practical use of magnetic fields and therapy of diseases related to functional deficiency of immunity. The methods of using them may be considerably broadened, particularly if it will be found that magentic fields are effective on processes of immunogenesis in peripheral lymphoid organs.

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STATUS AND PROSPECTS OF RESEARCH ON BIOLOGICAL AND THERAPEUTIC EFFECTS OF MAGNETIC FIELDS

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 pp 1-5

[Editorial by V. M. Bogolyubov, Central Scientific Research Institute of Balneology and Physiotherapy, Moscow]

[Text] In the first half of the 20th century, the problem of biological effects of magnetic fields (MF) drew the attention of only a few researchers concerned with the physiological aspect and general questions of therapeutic use of this factor. In connection with the advances in space biology and biophysics in the 1960's, there was a drastic increase in number of studies in this field. Their topics cover a wide range of questions, including therapeutic use of MF, magnetohygiene, magnetoecology, biomagnetism, etc. In recent years, the concept of biotropic parameters of MF was formed in magnetobiology, which refers to the physical characteristics of the field that determine the mechanisms of its interaction with biological systems, as well as biological effects. Intensity, gradient, vector, frequency and shape of pulses, as well as duration of exposure are among the main biotropic parameters of MF.

Induction of electromotive force (EMF) under the influence of static [stationary] (SMF) and variable (VMF) magnetic fields, as well as the effect of MF on the course of a number of free-radical chemical reactions in biological systems, have been provided with the most theoretical validation among the many physicochemical elements of the mechanism of action of MF. It has been demonstrated in many studies that SMF are capable of altering the speed of chemical reactions. This is based on the quantum mechanical patterns of interaction of MF with free radicals. Many works offer proof of the fact that SMF and low-frequency VMF affect processes of peroxidation of lipids in membranes and their permeability, and this could be one of the causes of their effects on proliferative and regenerative processes (V. M. Aristarkhov; Yu. A. Kholodov et al.).

Induction of EMF in flowing blood is one of the main mechanisms of action of SMF on the organism. Thus, R. P. Kikut showed that, when blood flows perpendicularly to the SMF lines of force, conditions are created in the region of positive potential for thrombosis and, conversely, for destruction of a

thrombus in the region of negative potential. The author used this effect on patients for thrombosing cerebrovascular aneurysms. It was demonstrated experimentally that under the prolonged effect of MF with over 60 mT induction there is shunting of arteriovenous anastomoses, which leads to sclerotic vascular changes and tissular hypoxia.

At the same time, there are a number of debatable questions in the study of primary mechanisms of MF effects. For example, the opinion is advanced that tunnel processes of electron and proton transfer play a special role in living systems (M. V. Vol'kenshteyn). Transfer of these charged particles could enhance sensitivity of biological systems to mild electromagnetic perturbations (M. A. Shishlo). On the other hand, there are reports that space charges, which are formed near the cell membranes and intracellular organelles, play an important part in the mechanism of action of MF. Resorption [dissipation?] of these charges alters the kinetics of transport processes in fine vessels, cells of different organs and tissues.

Formation of systemic adaptive reactions to local exposure to MF is among the important problems of magnetobiology and magnetotherapy. It was observed that redox processes and lipid peroxidation, as well as elements of the neuroendocrine system undergo changes under the influence of MF. It was established that, under the influence of MF, the nervous system can be involved in both the rapid and slow sensory system of initial reaction. The slow system is triggered under the influence of weak MF if exposed to them for a long time (Yu. A. Kholodov and M. A. Shishlo). In addition to the nervous system, the body's reaction to MF involves the endocrine glands. An increase in intensity of MF leads to stress reactions associated with release of ACTH, 11-hydroxycorticosteroids and activation of the sympathoadrenal system. Virtually all tested endocrine glands--hypothalamus-hypophysis-adrenal system, insular apparatus, thyroid and reproductive glands--were found to be sensitive to MF (N. A. Udintsev and S. M. Khlynin).

MF play a special part in altering immunological reactivity of the organism, and this explains their anti-inflammation action. This effect is most likely due to changes in blood coagulation and anticoagulation systems, improved microcirculation, as well as release of hormones, which increases immunological reactivity. This also determines the effects of MF on regenerative and repair processes. There is some link between the anti-inflammation and regeneration-enhancing effects of MF. This is probably attributable to the role of rheological properties of blood, effects on blood clotting, related change in tissular metabolism and, ultimately, change in immunological reactivity. The analgesic effect is most probably related to the anti-inflammation action of MF and is essentially secondary.

It can be stated that MF have an appreciable therapeutic action, and this has been indicated by virtually all researchers. This compels us to take a closer look at the mechanisms of therapeutic action of this factor, as well as to determine which forms of MF should be used for treatment of different diseases, with due consideration of magnitude of MF induction, gradient, vector, etc.

There are applications for MF in the treatment of such cardiovascular diseases as essential hypertension, ischemic heart disease (IHD), endarteritis obliterans and atherosclerosis, as well as chronic venous insufficiency. It was demonstrated at our institute that treatment of IHD patients with low-frequency VMF from a Polyus-1 unit, with induction of 9-19 mT attenuated or eliminated the pain syndrome in 55% of the cases. This factor was also shown to have a beneficial effect on acid-base balance of blood and physical load tolerance. No effect was demonstrable in cases of cardiac dysrhythmia, and this conforms with experimental data to the effect that MF influence primarily myocardial metabolism and contractility, but do not alter the heart's conduction system, in particular, the sinus node. At the same time, at our institute no appreciable clinical response was noted to treatment of IHD patients with elastic magnets with induction of 40 mT (the patients kept them in the region of the heart for 12 h/day).

Many studies were devoted to the effects of MF on peripheral circulation in the presence of arterial and venous insufficiency. There was improvement of parameters of blood coagulation, its rheological properties and, consequently, microcirculation of patients. There was normalization of colloid-osmotic pressure in microvessels, which was instrumental in disappearance of edema, improvement of oxygen transport and utilization in tissues (B. N. Zhukov et al.).

MF has had some effect on diseases of digestive organs. It was established at the Central Scientific Research Institute of Balneology and Physiotherapy that low-frequency VMF delivered from a Polyus-1 unit had a beneficial effect on peptic and duodenal ulcers. This was manifested by elimination or attenuation of pain and dyspeptic disorders in a significant part of the patients. A comparative study of the effects of this VMF to those of elastic magnets with 40 mT induction on the epigastric region revealed that the effect of the latter was considerably weaker. Thus, while healing of ulcers was observed in 64% of the patients treated with VMF, this applied to 50% with the use of elastomagnets.

To date, many data have been accumulated indicative of the beneficial effect of MF on postfracture bone union. Clinical, roentgenological, radioisotope and functional studies revealed that repair regeneration of bone occurs under more favorable conditions under the influence of MF, bone union and restoration of function in the injured limb occurred sooner. As shown by studies conducted at our institute, VMF with 30 mT induction intensified metabolic processes in regenerative bone, as manifested by earlier appearance of fibroblasts and osteoblasts. There was also faster elimination or attenuation of the pain syndrome and wider amplitude of movements in joints. In severe cases of arthrosis deformans and aseptic necrosis of the head of the femur, there was an increase in amplitude of movements in the joint under the influence of VMF treatment in the preoperative period, and this sometimes permits selection of a more sparing method of surgical intervention. Under the influence of VMF, there is increase in immunological reactivity in the presence of diseases of the joints and spine, normalization of lysozyme level and improvement of antibody-producing function of lymphocytes.

MF have a beneficial effect on a number of vascular diseases of the brain and peripheral nervous system. Treatment with low-frequency VMF was effective in

cases of polyneuritis; it was found to have an analgesic, trophic and spasmolytic effect, and improved the functional state of nerves. There are data to the effect that VMF are beneficial for the vertebrogenic radicular syndrome.

There are several reports of the beneficial therapeutic effects of VMF on diseases referable to the female reproductive system (V. M. Strugatskiy), ear, nose and throat (V. G. Chernykh and M. A. Malykh), eyes (L. V. Zobina et al.) and periodontosis (O. I. Yefanov).

While the therapeutic effect of VMF on many diseases has been proven, there is no agreement as to the effects of elastic magnets (magnetophores). Experimental and clinical studies of the effects of magnetophores at our institute failed to demonstrate an appreciable influence on blood coagulation or protein spectrum, osmotic stability of erythrocytes and other parameters. There was an insignificant response in cases of IHD, osteochondrosis of the spine, peptic ulcer, polyneuritis and fractures of the spine. At the same time, many authors have reported that similar magnetophores had a substantial effect on numerous diseases. As we see, it is imperative to work out standard criteria for assessing the therapeutic effects of this factor. Unfortunately, some of the researchers who reported the beneficial effect of magnetophores did not make comparative studies of a control group. Our scrutiny of the literature leads us to state that there were quite a few incidents where magnetophores were prescribed in conjunction with other therapeutic measures, and there were no control groups. Of course, such reports cause considerable confusion in the matter. We must expect that future studies will determine the true therapeutic value of magnetophores.

Evidently, new types of elastomagnets should be developed, which would be convenient for outpatient [ambulatory] treatment. Use of new ferromagnetic fillers permits development of elastomagnetics with higher maximum SMF induction on the surface and large dispersion fields.

The wide adoption of MF in health care practice depends largely on series production of equipment. At the present time, our industry produces the Polyus-1 unit; production of the Polyus-10 unit is at the preparation stage. At the same time, nonstandard equipment is being used in many institutions. We should distinguish among such equipment the units that generate pulsed MF that move ("slide") in space. One such unit was designed by Yu. V. Berlin et al.; it permits successive passage of MF pulses in the chain of the solenoid section. This unit produces pulsed MF with induction of 0.05 to 2.5 mT or more, with 1-1000 Hz pulse recurrence frequency. A modification of such a unit was designed by A. G. Yepifanov. Evidently, such MF should have more marked biological and therapeutic properties, since they interact with rather large volumes of tissues. In this regard, special mention should be made of the need to take into consideration the volume of tissues interacting with MF and its induction in comparative analysis of MF with different biotropic parameters. It should be stressed that heretofore no refined studies have been made for comparative analysis of the effects of MF with different biotropic parameters. Unfortunately, physiotherapy does not have at its disposal any good instruments for measuring MF induction, although this matter is one of the basic questions in scientific research.

Major advances have been made in recent years in the area of magnetobiology and magnetotherapy. Many aspects of the mechanism of action of SMF and VMF have been studied, and a clinical response has been noted for many diseases. A number of new pieces of equipment have been developed. The accumulated facts and other material should constitute a firm foundation for a combined [comprehensive] long-term specific program called upon to aid in continued progress in this field.

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DISTINCTIONS OF NERVOUS SYSTEM REACTIONS TO ARTIFICIALLY INTENSIFIED MAGNETIC FIELDS

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 (manuscript received 27 Feb 81) pp 5-9

[Article by Yu. A. Kholodov, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow]

[Text] A considerable number of publications have appeared in recent years in the world literature showing that all systems of the body can react to exogenous, intensified (as compared to natural) magnetic fields (MF). One can rank body systems in the following order, according to extent of involvement in reacting to total-body exposure to MF: nervous, endocrine, sense organs, cardiovascular, blood, digestive, muscles, excretory, respiratory, integument and bone. Presence of both local changes and reactions by systems not directly exposed to local MF compels us to believe that regulatory systems--nervous and endocrine--must be involved in reactions to MF. Without touching on many important problems of general magnetobiology, information about which can be gleaned from surveys (G. F. Plekhanov; Tenforde and others), we shall dwell on the distinctions of some reactions of the nervous system to MF. It must be noted that investigation of nervous system function under the influence of MF made it necessary to revise some established views on reactions elicited by ordinary stimuli.

We (Yu. A. Kholodov, 1966, 1975, and others) examined nervous system reactions to MF using psychophysical and psychophysiological methods for investigation of human nervous system function, as well as physiological, electrophysiological, conditioned reflex and histological methods in studies of nervous system activity of vertebrates and invertebrates. Preparations of the isolated nerve cord of the crayfish and neuronally isolated strip of rabbit cerebral cortex revealed that reactions to MF are more marked in isolated structures of the central nervous system than the intact brain.

Consequently, to the known reflex route of effects of stimuli on an organism is added, in the case of MF, the direct effect of this physical factor on structures of central regulation. This distinguishes the organism's reaction to MF from reactions to ordinary stimuli, such as light or sound.

Ultramicroscopic studies of the brain of animals exposed to MF revealed changes in mitochondria, synapses and membrane structures of the neuronal body. The

structure and function of the axons were found to be more resistant to MF than other subcellular elements. In this case, light microscopy revealed a primary neuroglial reaction (M. M. Aleksandrovskaya and Yu. A. Kholodov, N. L. Lazriyev and T. I. Kiknadze, and others), consisting of increased silver impregnation, which is related to the intensity of redox processes. Investigation of the direct response of the cerebral cortex to electric stimulation revealed involvement of neuroglia in physiological reactions of the brain to MF (S. I. Dumbadze et al.). The predominantly inhibitory effect of MF on conditioned reflex activity of animals can be related to its influence on neuroglia. The process of consolidation of memory trace was found to be the most sensitive to MF, followed by impaired formation of conditioned reflexes and, with intensification of MF there was a change in reproduction of other time associations.

Unlike the usual electroencephalographic desynchronization reaction, which occurs tenths of a second after exposure to a stimulus, MF elicited a diffuse EEG synchronization reaction, which appeared on the average 20 s after the start of exposure to MF. The parts of the brain we tested were ranked in the following order, according to intensity of this reaction: hypothalamus, cerebral cortex, thalamus, hippocampus, reticular formation of the mesencephalon. Administration of certain pharmacological agents could alter this order, which is indicative of dependence of reactions of different brain structures on their initial functional state. The EEG synchronization reaction was manifested by an increase in number of slow waves and spindles in electric activity of different parts of the brain, and on the behavioral level this was associated with prevalence of inhibitory processes.

However, MF could also stimulate the central nervous system: it was possible to develop a conditioned reflex to MF (true, it was less fixed than for light or sound) and to demonstrate sensory indications of MF in man.

As compared to the EEG reaction of the rabbit and sensory reactions of man to ordinary stimuli, the reactions to MF were characterized primarily by a long latency period, exceeding by about 10^2 the latency periods of ordinary reactions, as a result of which some researchers could not demonstrate an effect when they used brief exposure. Although variation of biotropic parameters of MF (induction, frequency, pulse shape, localization) did alter the latency period, it did not cause changes that would constitute a qualitative jump. In all cases, a distinctive slow system of early reaction was involved. The reaction lasted a mean of 10 s.

In offering detailed descriptions of this slow reaction system, one must take into consideration not only the main reaction, which is observed during exposure to MF, but the reaction to termination thereof, which appears about 15 s after discontinuing exposure (1-15 min) and lasts about 10 s.

The Table lists the main parameters of the slow and fast systems of initial reaction to exposure of the human head or hand to MF. We should call attention to the word, "initial," since other systems of slow adaptive reactions may become involved subsequently in the organism's reaction to any stimulus. Moreover, it should be borne in mind that the slow system of initial reaction is not directly related to the distinctions of the stimulus in question. For

example, exposure to variable MF could also elicit a reaction by the fast reaction system if it is directed at the retina. We are dealing with the magnetophosphene phenomenon, i.e., perception of a flash when the variable MF has induction in excess of a specific level (about 20 mT) at the subject's head. By analogy with this term, which is related to reactions of the system of rapid initial reaction, the sensory reaction related to the slow initial reaction system could be called "magnetocontact."

Comparative characteristics of some parameters of systems of rapid and slow initial sensory reactions of man exposed to variable MF

Parameter	System of rapid initial sensory reaction	System of slow initial sensory reaction
Latency period of simple motor reaction, s	0.2	20
Reaction time, s	0.5	10
Threshold induction of variable MF, mT	20	0.2
Modality of sensation	Phosphene	Contact

We are impressed the most with the 10^2 difference in the table in the latency period of the main reaction and the same difference in threshold sensibility between the two systems in question. Perhaps this is not a chance coincidence, and it is necessary to prolong exposure to the mild stimulus to enhance sensitivity. The threshold intensify of MF for a sensory reaction is close to that of earth's natural MF.

It is opportune to mention here that there are also slow (as shown in our experiments) and rapid systems of initial sensory reactions for SHF fields, but in the latter case we are dealing with auditory modality of sensing the SHF field. The modality of the slow initial system of sensory reaction to variable MF or SHF is similar, so that we could refer to distinctive "electromagnetic contact." The same "electromagnetic contacts" elicit a comparable diffuse EEG synchronization reaction in rabbits, which characterizes the slow initial reaction system, whereas ordinary stimuli elicit a rapid EEG desynchronization reaction.

Thus, the existence of slow and rapid systems of initial reactions was demonstrated in the analysis of reactions of the nervous system to two electromagnetic factors.

Because of the penetrating action of MF, we must refer to a new form of reaction, which could be called general alteration reaction, which stresses the general and simultaneous nature of effects of MF on biological processes. The details of this reaction are not yet clear, but we can note some of its distinctions. In man, it occurs most often on the subsensory level with triggering of the system of initial slow reaction. The similarity of reactions to local exposure on the periphery, with local exposure of the central nervous system and total-body exposure compels us to assume that the system of biologically active points is involved (Hsu and Fong).

The general alteration reaction differs from the usual one, which is initially effected through sense organs, in that there is simultaneous involvement of several systems of the organism in the reaction. The general alteration reaction to such a mild stimulus as MF is believed to be should elicit adaptive changes in the organism, which appear several minutes or hours after the start of exposure.

We did not observe summation of effects when 1-3-min exposure to MF was repeated after 10-20 min. This suggests that the initial reaction occurs within this interval. When exposure lasted more than 20 min, mice presented summation of effects as demonstrated by the conditioned reflex method. This phenomenon was observed with daily use of static MF for the above period of time. Hence, we can determine the duration of magnetotherapy sessions.

In general the organism's reactions to MF are notable for a long aftereffect. The result of 30-min exposure is manifested for 1 week and that of 6-h exposure for about 1 month. In this case, we are dealing with a reaction that can be called adaptive. While the initial reaction is limited primarily to sense organs and the nervous system, adaptation involves other systems in the response as well, first of all the endocrine system. From the practical point of view, we can discuss here the therapeutic use of MF. It has been learned that MF of diverse induction over a wide range of frequencies can elicit adaptive reactions in the organism that lead to increased resistance to infection, temperature, ionizing radiation, etc. As a result of such reactions, there may be activation of erythropoiesis, change in redox potential of tissues and changes in permeability of biological membranes. The lipoprotein complex of membranes is probably vulnerable.

Thanks to the work of M. A. Shishlo et al., Z. N. Nakhil'nitskaya et al., Yu. A. Kholodov and M. A. Shishlo et al., the idea of hypoxic changes is gaining increasing application when dealing with physiological mechanisms of MF action on the tissular level. It is opportune to note that the neuroglia is extremely sensitive to hypoxia.

L. Kh. Garkavi et al. expanded the stress theory of H. Selye, having introduced additional stages of the organism's general reaction to a stimulus of increasing intensity. According to the data of these authors, the triad that consists of conditioning, activation and stress reactions can occur several times when the intensity of the factor or its duration are increased, being expressed on different "levels" through an areactive zone. Such reactions can be produced by exposure of the hypothalamic region to MF.

When duration of exposure to MF is prolonged considerably, the adaptive reactions of the organism could change into pathological ones related to destructive changes in neurons. However, all of the studies stress the reversible nature of changes in the nervous system. Although this system is the most sensitive to MF, it is the least stricken, as compared to the endocrine system, for example.

Thus, we can list among the distinctions of nervous system reactions to MF a multitude of physiological mechanisms of expression of effects (direct and

reflex action with involvement of slow and fast reaction systems), high sensitivity to MF of higher centers of autonomic regulation of functions, involvement of neuroglial elements and prevalence of inhibitory processes in formation of the response. Continued investigation of the above distinctions in the nervous system's reactions to MF will permit demonstration of some new properties in the nervous system and strengthen the theoretical bases of magnetotherapy.

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MECHANISM OF BIOLOGICAL EFFECTS OF MAGNETIC FIELDS

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 (manuscript received 13 Feb 81) pp 9-12

[Article by N. A. Udintsev, Department of Biochemistry (headed by Prof N. A. Udintsev), Tomsk Medical Institute]

[Text] Magnetic fields (MF) of different intensities and frequencies are being used more and more extensively for treatment of diseases of the skeletomuscular system, vessels and gastrointestinal tract. However, there is still insufficient theoretical validation of their use.

It is known that MF have a marked influence on the integral organism, less on isolated organs and particularly pure enzymes. This is attributable to the role of the neuroendocrine system, which can convert a signal of infinitesimal energy into a powerful adaptive metabolic chain reaction; for this reason, the mechanism of biological effects of MF, like other physiotherapeutic factors, should be investigated from the standpoint of systemic organization of functions.

For several years a combined study has been in progress at our institute of the state of the neuroendocrine system and metabolism after total-body exposure of white rats to variable MF (VMF) with 20 mT induction and at a frequency of 50 Hz, i.e., close to the technique often used for therapeutic purposes. We submit here some of the data obtained primarily in the case of brief exposure, which are of greatest interest to physicians.

As we know, the pituitary-adrenal system plays a leading role in the mechanism of adaptation to the effects of the most diverse factors. In order to assess the functional state of elements of this system, we assayed ACTH by the radioimmunological method and 11-HCS [hydroxycorticosteroids] by the fluorimetric method, as well as a number of other parameters.

It was established that when a magnet is turned on and immediately turned off, as well as with exposure to VMF for 3-5 min, there is no appreciable change in blood HCS content; when exposure is extended to 7-8 min this level increases by 38% and after 10-15-min exposure it almost doubles. The increase in steroid content occurs mainly at the expense of free forms of the hormone, with some increase in degree of transcortin saturation (V. V. Moroz, 1979; N. A. Udintsev and V. V. Moroz).

Studies of the reaction of the central element of the hypophyseoadrenal system revealed that there was substantial increase in ACTH content of the pituitary (by 60%) and blood (by 73 and 100%) (V. V. Moroz, 1979) in response to brief (5 and 15 min) exposure to VMF, and this indicates, once more, the sensitivity of this part of the brain to MF. The fact that 11-HCS content of blood did not change in response to VMF after hypophysectomy is indicative of the determinant significance of the pituitary (N. A. Udintsev and V. V. Moroz).

As a result of investigation of the triggering mechanism and significance of various factors in development of the reaction to VMF, it was established that α- and particularly β-receptors play an important role (V. V. Moroz, 1977), and that the functional state of the central nervous system and higher branches of the neuroendocrine system, levels of reserve catecholamines and functions of the adrenal medulla were important (S. A. Sakharov).

At the same time, the impression is formed that the nature of the reaction to MF is different for different parts of the hypothalamohypophyseal region. Thus, histological examination of the pituitary after exposure to MF with induction of 40 mT and at a frequency of 1 Hz of the region of the head, greater gonadotroph and lesser thyrotroph activity were noted (Yu. N. Bordyushkov et al.). According to our data, immediately after 15-min exposure to VMF with 20 mT induction and frequency of 50 Hz there was no appreciable change in functional state of the thyroid. It is only after 1 h that its cAMP level rose due to increased production of thyrotropic hormone. In the interval between 4 and 7 h, there was significant elevation of level of protein-bound radioactive iodine in blood (by 86.5%), which reverted to normal only after 2 days. There was appreciable increase in total thyroxine content (T_4) in blood after 12 h and elevation of effective thyroxine index with decrease in binding capacity of thyroxine-binding globulin (V. Yu. Serebrov). Stimulation of neurosecretion from the supraoptic nucleus was noted 1-2 h after exposure to static MF with 1-10 mT induction for 5 min, and such stimulation for the paraventricular nucleus occurred even later (S. A. Vashurina).

Thus, the preliminary conclusion can be made that the biological effects of MF on the integral organism are largely determined by the nature of reactions of higher branches of the neuroendocrine system. Stimulation of this region elicits a chain reaction of activation of target endocrine glands, followed by numerous ramified metabolic reactions.

Evidently a typical distinction of MF is its stimulating effect on thyroid function, unlike the inhibitory effect of many other stimuli.

The biological effects of MF are manifested with exposure not only of the head region but with local delivery to various parts of the body, as is the case when used for therapeutic purposes. Evidently, in this case the functional state of the hypothalamohypophyseal region is important.

Secondary transmission of the hormonal signal is effected by the adenyl and guanyl cylase system. We have demonstrated that there is statistically reliable increase in cGMP content of the liver and heart (N. A. Udintsev and V. V. Ivanov) and cAMP in the thyroid (V. Yu. Serebrov) in rat organs and tissues after 15-min exposure to 20 mT VMF.

The existing data suggest that, as a result of systemic endocrine gland reaction, numerous metabolic reactions are triggered. Apparently, they are not fully balanced at first; however, they perform the main physiological role in enhancing resistance of the organism, since they are aimed primarily at preserving energy homeostasis. This is indicated by data on activation of enzymes of glycolysis and processes localized in mitochondrial membranes, which are the most sensitive structures of the cell (N. A. Udintsev and N. V. Kanskaya).

There is a substantial change in parameters of lipid metabolism: increase in levels of nonesterified fatty acids and phospholipids in blood, liver and myocardium (N. V. Kanskaya).

It can be assumed that metabolism rapidly switches from the carbohydrate to lipid type under the influence of MF. Evidently, activation of hormone-sensitive lipase of adipose tissue, as a result of rise in corticosteroid level, plays some part in this process.

Activity of α-glycerophosphate dehydrogenase of cytoplasm and mitochondria, referable to thyroxine-sensitive dehydrogenases, as well as succinate dehydrogenase and cytochromoxidase, was examined to assess some of the metabolic factors linking processes of carbohydrate and lipid metabolism. It was established that, in spite of the unchanging thyroid hormone content, there was substantial activation of mitochondrial α-glycerophosphate dehydrogenase in the myocardium (unlike the liver and spleen) after 15-min exposure to VMF, apparently due to stimulation of glycolysis and lipolysis. Activity thereof in the liver increases in accordance with increase in blood thyroid hormone content; such a correlation was not demonstrable with regard to dynamics of succinate dehydrogenase and cytochromoxidase activity (V. Yu. Serebrov).

The suggestion that there is activation of lipid peroxidation is one of the hypotheses that explains the mechanism of MF effects. However, unlike the findings with prolonged exposure, no appreciable changes were demonstrable after brief exposure to VMF (20 mT, 50 Hz) with regard to levels of lipid peroxides, diene conjugates and malonic dialdehyde in the liver, and chemiluminescence even diminished (V. V. Ivanov); there was no increase in amount of peroxides in erythrocytes either (I. A. Serebrennikova and V. A. Ushakov). Probably, there was no significant activation of peroxidation processes with brief exposure to VMF, and the extent of antioxidant protection was sufficient to prevent accumulation of peroxides.

Extending exposure to several hours and numerous repetitions thereof elicit a different effect: depression of hypophyseoadrenal system function (N. A. Udintsev, and V. V. Moroz), insular system (N. I. Kolesova et al.), testes (N. A. Udintsev and S. M. Khlynin), and only thyroid activity remains high (V. Yu. Serebrov). There is depression of respiratory enzyme activity and impaired energy supply to tissues (N. A. Udintsev and V. V. Moroz, N. A. Udintsev and S. M. Khlynin). Microcirculatory changes are important in the genesis of these disturbances.

It is important to have knowledge about the dynamics of processes in the recovery period following exposure to MF in order to make purposeful use thereof. For example, 11-HCS content of blood reverts to normal within 2 h after exposure for 15 min to VMF (20 mT, 50 Hz). However, if the interval between treatments is reduced to 30 min, the reaction to each successive exposure to the magnet diminishes and after the 4th-5th exposure the 11-HCS level of blood remains unchanged (V. V. Moroz, 1979).

Thus, the beneficial therapeutic effect of VMF when used for brief treatments has a complicated genesis and is determined by its significant stimulating effect on the neuroendocrine system, activation of carbohydrate and lipid metabolism. This direction of tissular metabolism can be interpreted as a "conditioning" or "activation" reaction (L. Kh. Garkavi et al.).

It is imperative to continue with in-depth investigation of the mechanism of MF effects on all levels of organization, preferably on models of various pathological states.

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FORMATION OF SYSTEMIC ADAPTATION REACTIONS IN STATIC MAGNETIC FIELDS

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[Article by M. A. Shishlo, S. Kh. Kubli and L. L. Shimkevich, Central Scientific Research Institute of Balneology and Physiotherapy, Moscow]

[Text] There is activation of compensatory and adaptive processes, as well as formation of systemic adaptive reactions that enhance resistance to deleterious environmental factors, with exposure to magnetic fields that have adequately selected parameters.

In our studies, which involved brief (30 min) daily exposure of animals (rats) to a static magnetic field (SMF), 50 mT, when a rather large volume of tissues was involved in interaction with the field, we observed a reliable increase in dispersion of resistance without reliable change in its mean level after two SMF treatments. By the 8th-9th day (6-7 treatments), there was reliable increase in resistance of the entire animal population. By the 18th-19th day (14-15 treatments), resistance diminished, while dispersion of resistance decreased substantially, as compared to the control. The Table illustrates an example of this. Under the influence of many weeks of exposure to magnetic fields (MF) fluctuations of these parameters persist but their amplitude gradually disappears (L. Kh. Garkavi et al.; V. N. Fatenkov and N. A. Klenova), which reflects habituation to this factor.

After 6-7 SMF treatments, we observed not only an increase in systemic resistance to hyperoxia, but depression of destructive processes induced by reserpine in the gastric mucosa and increase in anti-inflammation potential of the organism (Yu. A. Kholodov, M. A. Shishlov).

A scrutiny of time organization of slow fluctuating changes in systemic resistance adds some clarity to the mechanism of appearance thereof. With exposure to SMF as indicated above, 11-HCS [hydroxycorticosteroids] content of blood increased insignificantly after 2 treatments, then decreased to below the initial level by the 6th-7th and reverted to the base level in the 14th-15th treatment. Analogous in-phase ["synphasic"] fluctuations were found in adrenal epinephrine, norepinephrine and dopa content, but not in brain tissue, under the influence of SMF. Reliable differences were demonstrable only in dynamics of the fluctuations, but not absolute levels of parameters, as compared to the control (pseudotreatments).

Effect of SMF on animal resistance to toxicity of oxygen at pressure of 6 atm.(abs.)

Experimental conditions	Development of severe oxygen toxicity, min				
	n	$\overline{M}\pm m$	σ	F	P
Control (intact animals)	23	35,5±2,50	11,98	—	
SMF:					
2 treatments	9	38,6±5,84	17,52	$F=2,14$ $F<F_{05}$	—
7 "	14	43,8±3,04	11,37	—	$t=2,13$ $P<0,05$ $Q=12$
15 "	9	33,6±1,79	5,39	$F=10,59$ $F>F_{01}$	—

Key: F) Fisher's criterion
P) reliability of differences from intact animals (*t*--Student-Fisher criterion; Q--nonparametric Rosenbaum criterion)

Brain tissue norepinephrine content did not change appreciably, but there was a distinct tendency toward decline of epinephrine and reliable decline of dopa level in the 6th-7th treatment, which persisted as a tendency in the 14th-15th treatment as well.

We observed an increase in area of medullary substance of thymus lobes (485±49 µm versus 234±56 µm in diameter) after 2 exposures to SMF and negligible dystrophic changes in its stroma. At the same period there was marked migration of lymphoid elements into liver tissue. After 6-7 treatments, there was a reliable increase in weight of the thymus, area of medullary substance of lobules which was increased, as before (406±41 µm). At this time, the gland presented intensified lymphopoiesis and increase in number of mast cells. By the 14th-15th exposure, the weight of this gland, as well as area of lobular medullary substance, reverted to control values (256±66 µm in diameter), but the dystrophic changes persisted in stromal reticular cells. At this time, there was an increase in eosinophil content over the periphery of the gland and in its capsule. It must be stressed that there were changes in condition of capillaries after 2 treatments: dilatation and plasma saturation of walls of fine vessels, which persisted up to the 6th-7th treatment and disappeared only by the 14th-15th exposure to SMF.

We also demonstrated fluctuating changes in bioenergetics, as assessed by polarography of mitochondria isolated from the liver. They were manifested the most distinctly in the parameter of respiratory control of glutamate (RCgl), which reflects inhibition of succinate dehydrogenase (SDH) by oxalacetic acid, the degree of which increases with de-energizing of mitochondria. Thus, RCgl in dissociate state of mitochondria increased to 1.17±0.05 in the 2d treatment, dropped to 0.99±0.03 in the 6th-7th and rose again to 1.05±0.03 by the 14th-15th treatment. Typically enough, during the second exposure to SMF there was substantial increase in dispersion of α-ketoglutarate oxidation rate ($F>F_{01}$),

Tissular bioenergetics reflect, in a sort of mirror image, the neuroendocrine status of the organism. In view of the fact that maximum increase in animal resistance was observed with the 6th-7th treatment, it was interesting to make a more comprehensive study of bioenergetics in this period.

After 6-7 SMF treatments, liver mitochondria presented mild inhibition of succinate oxidation and concurrent decline of RCgl in the third metabolic state according to Chance, which is indicative of diminished SDH inhibition by oxalacetic acid. There was a decrease in rate of oxidation of the NAD-dependent malate substrate, particularly in the controlled state after termination of ADP phosphorylation ($P<0.01$). No appreciable changes were demonstrated in α-ketoglutarate oxidation in samples with ADP, and we merely noted a tendency toward decline of ADP/O ratio. At the same time, there was increased inhibition of malate oxidation by α-ketoglutarate in the presence of DNP and the ATPase inhibitor, dicyclohyexyl carbodiimide (DCCD). This was indicative of increased GTP production in hepatic mitochondria and could serve as the basis for inhibition of oxidation by NAD-dependent substrates (Figure 1). The latter activates the malate-aspartate shunt and reflects in rats intensification of gluconeogenesis and nucleic acid synthesis in the liver (Ye. A. Kosenko et al.; Ye. I. Mayevskiy and M. N. Kondrashova; Olson and Allgyer).

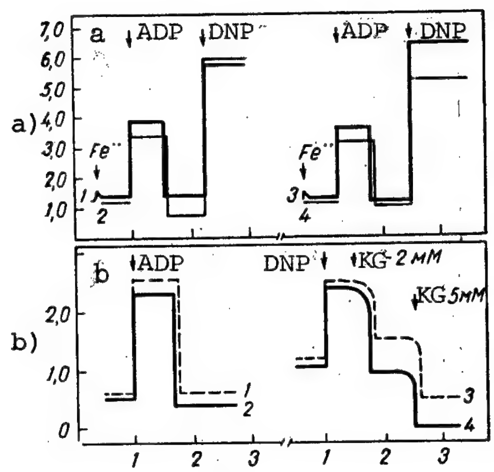

Figure 1.
Functional state of liver mitochondria after 7 treatments with SMF, 50 mT. X-axis, time (min); y-axis, respiratory rate (in n-atom O/s)

a) 1, 2) control 3, 4) experiment
Substrate: 10 mm succinate, 230 μM ADP, α = 2,4-dinitrophenol (DNP)--30 μM. Saccharose-magnesium incubation medium, pH 7.4; 3 mg mitochondrial protein in sample. 1, 3) with addition of $FeSO_4$ (50 μM); 2, 4) without such addition

b) 1, 3) control 2, 4) experiment
Substrate: malate (2.5 mM) + glutamate (2.5 mM); 1, 2) saccharose-magnesium incubation medium, 3 mg mitochondrial protein; 3, 4) incubation medium (mM): saccharose--200, KCl--50, tris-HCl buffer--10, potassium phosphate--2, EDTA--1, pH 7.3, DCCD--50 μM in medium; KG--α-ketoglutarate; 6 mg mitochondrial protein

At this stage, there was a decrease in dissociating effect of adding Fe^{2+} ions to the mitochondrial incubation medium. This is indicative of depression of processes of lipid peroxidation and possible decline of endogenous nonheme iron (Fe_{nh}) level in liver mitochondria, which correlates with increased animal resistance to hypoxia after 6-7 exposures to SMF. At the same time, the decrease in nonheme iron content could play a part in lowering ATPase activity of mitochondria, which is instrumental in changing their metabolism to maintain synthesis of phosphoenol pyruvate and gluconeogenesis.

By the 8th-9th day of exposure to SMF, there was development of a set of related changes in neuroendocrine status and tissular bioenergetics, in the form of inhibition of peripheral β-adrenoreceptors and decreased activity of the central element of the sympathoadrenal system, low blood glucocorticoid level and inhibition of lipid peroxidation processes, alteration of liver bioenergetics in the direction of prevalence of a number of biosynthetic processes and activation of lymphopoiesis in the thymus. All this is consistent with the adaptive reaction of conditioning (L. Kh. Garkavi et al.) and satisfies the necessary conditions to avert pathological processes provoked by stress reactions (F. Z. Meyerson).

The adaptive reaction formed under the influence of SMF is of the greatest interest to the study of recovery processes. For this reason, the key question is the mechanism whereby a mild biological stimulus, such as SMF, causes a change in compensatory and adaptive processes.

De-energization of tissue (increased entropy in the target system), the rate and degree of which determine the force of the factor as a biological stimulus, is a mandatory property of the stimulus when it interacts with a biological system (M. A. Shishlo and M. N. Kondrashova). SMF is characterized by low rate and degree of de-energization, thanks to which it is impossible for direct activation of the rapid reaction system (Yu. A. Kholodov and M. M. Shishlo) with input into central mechanisms of hypothalamo-hypophyseal regulation. Then the question logically arises as to which trigger and which information channel are involved in signaling interaction between the organism and SMF causing subsequent alteration of adaptive mechanisms.

Cellular and noncellular constituents of blood, its clotting system (R. P. Kikut) and vascular endothelium, the involvement of which in reactions to SMF have been long since reported (M. A. Shishlo) and has presently undergone further development, play a leading part in the reactions to SMF. The significant nonlinearity of reactions of the blood coagulating system and conjugate cooperation in the behavior of vascular endothelium form the specific properties of this trigger and determine its role in regulation of physiological processes exposed to SMF.

In the case of extreme, stress-producing factors, blood coagulation is determined by the neuroendocrine status and triggering, signaling significance of the clotting system is depressed.

There is the opposite correlation between these systems under the influence of mild biological stimuli, in particular, SMF: the hemostasis system causes alteration of neuroendocrine regulatory mechanisms.

By changing the colloid state of cellular cytoplasm and ATPase activity of cell membranes, the blood clotting system has a direct bearing on regulation of charge asymmetry of cells. Charges are separated ($\bar{e}$ and H^+, Na and K) in biological membranes and we observed crossing over of the two chief mechanisms of integration of cellular and tissular processes, one of which is based on the wave, frequency properties of supramolecular structures and the other, on informative properties of substances of biological origin, such as cyclic nucleotides, antigenic properties of membranes, etc. (Yu. A. Kholodov

and M. A. Shishlo). The change in charge asymmetry of cell membranes consistently leads to conjugate change in intracellular metabolic processes and, perhaps, antigenic properties of plasma membranes.

On the other hand, it is known that direct electric perturbation specifically alters the blood and tissue clotting system.

Thus, there are both direct and feedback ties between the hemostasis system and charge asymmetry in blood and tissue cells, which makes this functional system rather independent and, probably, related to the presence of biologically active points.

The depth and basic nature of the relationship between these phenomena are indicated by the fact that acetylsalicylic acid, which is known as an anti-inflammation and antipyretic agent, also has the properties of an anticoagulant and dissociating factor for oxidative phosphorylation, i.e., it eliminates charge asymmetry of mitochondrial membranes--lowers the electrochemical potential of hydrogen ions on the membrane and activates ATPase. Let us mention that anticoagulants of the dicoumarin type (indirect action) are also classical "disconnectors" of oxidative phosphorylation in mitochondria.

The foregoing is all the more meaningful, since MF are capable of releasing charge asymmetry of membranes and, in particular, mitochondria, both directly and indirectly through induction of electromotive force. Here, tunnel mechanisms of charge transfer are of prime significance, and they determine the macroscopic characteristics of interaction between magnetic fields and biological systems (Yu. A. Kholodov and M. A. Shishlo).

The slow system of reaction to MF in question has outputs for modulation of the main neuroendocrine mechanisms of maintaining homeostasis by altering sensitivity of membrane receptors to nervous system mediators, change in bioenergetics, biosynthesis of prostaglandins, immunological reactivity and other effects.

Let us offer just one example of how the "perturbation" caused by SMF in the blood clotting system is reflected in the immunological system. Either the body or tail of rats was exposed to SMF. In the latter case, induction of electromotive force in blood flow in caudal vessels and a corresponding change in the hemostasis sytem were the biologically significant mechanism of SMF effects.

In young animals (rats weighing 130-170 g), a reliable decrease in weight of the thymus was obtained with both localizations of exposure after two such procedures. In larger animals (weighing 180-240 g), two exposures of SMF to both localizations elicited a marked tendency toward increase in mass of this gland. However, subsequent kinetics of changes in the gland with increase in number of exposures to SMF (30 min daily) depended on the localization of exposure: there was "eluding" of SMF with exposure of the tail; with exposure of the body, the effect of SMF grew by the 7th treatment (Figure 2). These differences are largely related to the volume of tissue interacting with the field, i.e., degree of "perturbation" brought into the hemostasis system.

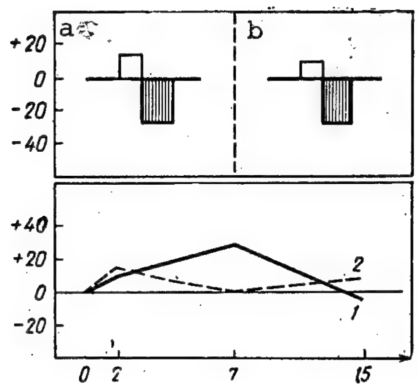

Figure 2.
Change in weight coefficient of thymus (% of control) as related to localization of SMF. Top: animals of different weights (and age) after 2d exposure to SMF. Cross-hatched columns--weight 130-170 g ($P<0.05$); white columns--180-240 g ($P<0.1$). Localization of SMF: a) on tail; b) body. Bottom: numerous exposure to SMF of rats weighing 180-240 g (number of treatments shown on x-axis). Localization of SMF: 1) body; 2) tail

The obtained data are indicative of the role of the hemostasis system and charge asymmetry of cell membranes in formation of antigenic properties of tissues and possible peripheral regulation of immunological reactivity. The rise in autoantibody level under the influence of SMF, which was repeatedly demonstrated by researchers, should also be interpreted in this light.

Synchronization of intracellular processes by means of "perturbation," caused by drop of charge asymmetry of membranes through change in the blood clotting system should be considered the cause of appearance of macroscopic fluctuations of mechanisms involved in maintaining homeostasis, on the basis of the properties of the slow trigger system of reacting to SMF. The asynchronous course of intracellular processes in large volumes of peripheral organs under the influence of SMF is split into several main oscillatory elements, and this is associated with synchronization of processes of de novo replenishment of intracellular structures and long-period oscillation ["swinging"] of functional ties between different elements of homeostasis mechanisms. It is remarkable that the 10-day term corresponds to the half-life of renewal of mitochondria in the liver, and in our experiments the half-life of the oscillatory cycle in homeostatic systems noted under the influence of SMF was close to this term--8-9 days (6-7 treatments). Such "swinging" of homeostatic systems is in essence a manifestation of changes in time and space organization of integration processes in regulatory systems of the integral organism, and it permits disclosure of the functional ties between different elements of the system of maintaining homeostasis. Thus, during the second exposure to SMF, a positive relation is demonstrable between de-energization of liver mitochondria and activation of α-ketoglutarate oxidation, migration of lymphoid elements in the liver and mild activation of the peripheral part of the sympathoadrenal system. By the 6th-7th treatment, there is a positive relation between activation of synthesis of phosphoenol pyruvate (activation of gluconeogenesis) in the liver and lymphopoiesis in the thymus against a background of low blood 11-HCS, etc. The result of comparing these data serves as more evidence of the fact that cellular bioenergetics serves as a most important element of integration in the center--periphery system, and it is contained as a most important component in the mechanism of formation of biological rhythms.

The synchronization phenomenon may have important applied implications with regard to stimulation of regenerative processes; at the same time, when it is necessary to maintain a state of high system resistance for a long period of time it is undesirable. Variation of biotropic parameters of MF in the course of a long series of treatments (variation of intensity and frequency of MF, localization of treatment) helps eliminate this phenomenon (L. Kh. Garkavi et al.). All these procedures are aimed at desynchronization of integration mechanisms, i.e., preservation of the numerous oscillatory components in the homeostatic system and use of different levels of organization in triggering processes for formation of adaptive reactions. However, the effects of MF are still based on the same mechanisms, with the involvement of tunnel processes of regulation of charge asymmetry of cell membranes.

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POSSIBLE USE OF MAGNETOBIOLOGICAL EFFECTS IN NEUROSURGERY

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 (manuscript received 22 Jan 81) pp 18-24

[Article by R. P. Kikut, M. E. Liyepa, G. A. Kruminya, S. R. Kikute, E. A. Vitols and D. L. Apshkalne, Riga Medical Institute]

[Text] For the last 10 years, there have been intensive studies of the use of magnetic fields (MF) in neurosurgery, which were pursued at the Riga Medical Institute and Riga Scientific Research Institute of Traumatology and Orthopedics. Special scientific teams and a laboratory were formed there to explore the possibility of using magnetobiological effects in the presence of neurovascular, neurooncological and inflammatory diseases of the central nervous system involving adhesive and glial processes. By investigating the biological effects of MF, we are developing new methods of treating neurosurgical patients, which could supplement or replace existing surgical methods.

Data on the use of MF in neurosurgery are furnished in the article of Alksne et al., but they only used the magnetic property of attracting ferromagnetic particles.

Joint studies of physicians and physicists discovered a previously unknown phenomenon, the occurrence of immediate hematological changes in flowing blood during exposure to a static MF (SMF): as blood passes through a vessel that is perpendicular to the vector of SMF induction, particles of blood in one half of the vessel acquire a stronger negative charge and in the other half, on the contrary the charge of particles could exceed the isoelectric point and become positive. On opposite sides of the vessel different clotting conditions are created, which are based on the bioelectric phenomenon (Sawyer and Pate) induced, in our cases, by SMF. Thus, we have demonstrated that the vector of SMF induction effects its biological action through the blood under certain conditions (Figure 1).

We investigated the thrombus-forming effect on the side of positive induction of a blood vessel in experiments with artificial aneurysms. In addition to changes in parameters of the coagulation system and in number of blood cells, we recorded induced biopotentials of blood in the segments of the vessel perpendicular to the induction vector of SMF.

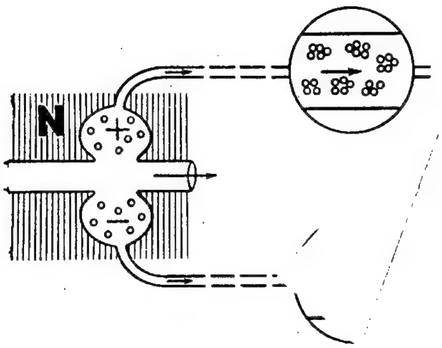

Figure 1.
Occurrence of hematological changes in moving blood, in a static magnetic field
+) side of positive induction, hypercoagulation changes in blood
-) side of negative induction, hypocoagulation changes

On the basis of the obtained data it has become possible to control thrombus formation in cerebrovascular aneurysms using a no-contact method and, in a number of cases, to replace intracranial operations with guided MF.

At the present time, three original units have been developed in neurosurgical clinics of Riga, which permit delivery of strictly guided SMF differing in induction to cerebral vessels (Figure 2 [photo not reproduced]). A technique was developed for thrombosing aneurysmal vessels (R. P. Kikut and D. K. Miller) in an 0.15-0.25 T SMF. The parameters of the blood coagulating system are monitored before and after using SMF. The patients' angiograms serve as a control.

These SMF Units were used in the treatment of 53 patients with aneurysms of cerebral arteries. Angiography was indicative of reduction in volume of the aneurysmal sac, i.e., strengthening of the wall of the aneurysm or complete closure of its lumen (Figure 3 [photo not reproduced]).

The desirability of using this method is proven by the favorable follow-up history (over 7 years, 3 patients), as well as beneficial effect in other patients followed up for long periods of time. Of the 53 patients, 38 have returned to active work, 12 are living; 3 expired (2 due to intracerebral hemorrhage and 1 due to head trauma).

Use of this method of treating aneurysms of arterial vessels of the brain can be considered indicated when it is impossible to operate (awkward localization of aneurysm, intercurrent disease, advanced age of patients).

The opposite effect of SMF is also used in clinical practice: elastic, implantable magnetic cuffs have been developed at the All-Union Scientific Research Institute of the Rubber Industry to prevent thrombus formation. The Magnetic cuffs with induction of 0.015-0.020 T have been used in vascular surgery, particularly in the presence of stenosing processes in the basin of the common carotid arteries. Clinically, this group of patients was characterized by transient cerebrovascular disturbances in the carotid basin, occasional ischemic insultus appearing several months before surgical intervention.

In all, 39 operations were performed involving unilateral adventectomy for stenosis of carotid basin vessels followed by application of a guided magnetic cuff on the trunk of the common carotid, which was attached to the vascular wall with a few fine silk sutures.

In 26 patients, there was significant attenuation or disappearance of transient cerebrovascular disorders within 1 year after surgery, as well as less marked organic symptoms resulting from the previously sustained ischemic insultus. In 10 patients (chiefly those presenting marked postinsultus organic changes) there was no improvement. We observed some tendency toward attenuation of the thrombus-forming process in operated patients according to the usual clinical tests. In three patients, an operation of this type was associated with dissection of the vascular wall and removal of a large atherosclerotic plaque. Three patients who presented marked bilateral carotid and vertebral pathology with recurrent cerebral ischemia expired within 2 months after surgery.

Thus, this type of operation was effective in cases of incipient insultus. It can be performed when it is impossible to perform endovascular operations and as a preventive measure to prevent thrombus formation during surgical interventions.

Subsequently, MF were used in neurosurgical practice in cases of neuro-ophthalmological pathology.

It was known from the literature that variable low-frequency (50 Hz) MF (VMF) have an anti-inflammation effect, enhance nonspecific systemic resistance, improve microcirculation and tissue trophics (L. Kh. Garkavi et al., 1978); for this reason we tried to use VMF for optochiasmal leptomeningitis.

At the acute stage of this disease, inflammatory changes are demonstrable pathomorphologically at the base of the brain in its arachnoid and vascular meninges and adjacent brain matter around the optic nerves and optic decussation (O. N. Sokolova). Clinically, this is manifested by a decrease in visual acuity to virtual blindness, which is related to appearance of gross defects in the visual fields. When the acute stage changes into a chronic one, connective tissue adhesions and cysts form in the meninges around the optic nerves. This results in further decline of vision, atrophy of optic nerves and blindness.

With the use of known conservative methods of treating optochiasmal leptomeningitis a total cure is relatively seldom observed (20-30% of the patients), and for this reason we tested the possibility of using VMF from the Soviet-made Polyus-1 unit as a therapeutic factor. Field induction (10 to 40 mT) and duration of treatment (2 to 15 min) depended on the patient's individual reaction (degree of improvement of vision, activation of white blood cells, well-being). The patients underwent 1 to 3 courses of magnetotherapy, each consisting of 12-15 treatments.

Prior to treatment, visual acuity was below 0.1 (ranging from light perception to 0.09) in all 18 patients examined, and there were mainly centrally localized defects in the visual fields differing in size (2 to 35°); the patients could not read, write, etc. We succeeded in maintaining the reaction of activation of blood according to L. Kh. Garkavi et al. by means of magnetotherapy; there was also improvement in well-being, sleep and in 16 patients in vision. This is attributable to reduction of inflammatory phenomena in the meninges, as indicated by normalization of spinal fluid, reduction (in 9 cases) or disappearance (in 7) of visual field defects; visual acuity of all

these patients improved (to 0.4-0.8 in 6 cases, 0.2-0.3 in 6, 0.02 to 0.1 in 4 cases). The patients were able to read and write.

The outcome of VMF treatment dependend on duration of disease (best results were obtained when it was present for no more than 3 months).

Thus, VMF can be used in expressly the acute stage of optochiasmal leptomeningitis.

Use of MF in neurooncology was also a new direction of medical magnetobiology.

Studies of recent years revealed that a state of heightened nonspecific systemic resistance develops under the influence of MF of a specific intensity (L. Kh. Garkavi et al., 1977). In the course of experiments on animals with tumors it was demonstrated that VMF in doses that elicit a nonspecific systemic reaction attenuate the deleterious effects of chemotherapy and radiation therapy without lowering the antineoplastic effect.

We used VMF to improve tolerance of massive doses of multiple chemical agents by patients with malignant glial tumors of the brain. A number of toxic side-effects (impairment of neuropsychological status in the form of depression, sleep disorders, loss of appetite, heightened emotional lability) develop in patients under polychemotherapy, and there is inhibition of hemopoietic processes.

Patients with malignant neuroglial tumors of the brain are treated at the Riga Republic Neurosurgical Center with a course of polychemotherapy consisting of individually selected chemotherapeutic agents. From the first day of chemotherapy we also used VMF. The inductors of the Polyus-1 unit were applied symmetrically on both sides to the parietal regions. Treatments were given daily for the entire duration of the course of multiple chemotherapy, increasing duration from 5 to 15 min (depending on hematological parameters and clinical symptoms). We counted the absolute number of lymphocytes and monocytes per microliter blood (mononuclear index). A blood transfusion was prescribed if this index dropped to less than 1500/$\mu\ell$. We took an EEG and determined the patients' neuropsychological status at the start and end of the course of therapy.

Magnetotherapy was administered to 43 patients with malignant glioma. The control group consisted of 28 patients with malignant glioma who had received polychemotherapy along with vitamins and the biostimulator, eleuterococcus. These patients developed side-effects (marked psychodepressive syndrome and EEG changes in 69%, drop of mononuclear index of peripheral blood in 77%), so that the complete course of polychemotherapy could not be given. It was necessary to give blood transfusions to 75% of the patients.

With the use of multiple chemotherapeutic agents and magnetotherapy, it was possible to give all 43 patients a complete course of drug therapy and reduce blood transfusions to more than one-fifth, as compared to the control group, and they did not develop any pronounced neuropsychological side-effects. Most of them were in higher spirits, presenting some euphoria, their sleep and appetite improved; depression of the mononuclear index was observed in 63% of the patients.

The course of combined treatment of patients with glial brain tumors using the method we developed was repeated every 3 months. We found that mean survival time of such patients constituted 22.4 months, whereas it did not exceed 9 months with surgical management alone, according to the data of A. N. Konovalov and A. P. Romodanov.

A tomographic-computer recheck of the brain of patients treated by the new method revealed that growth was arrested and, in some cases, the size of the malignant tumor diminished.

Thus, according to our observations, VMF enhances tolerance of massive doses of multiple chemotherapeutic agents and improves the results of treating patients with malignant glial tumors of the brain.

We also tested the efficacy of SMF on human glial tumors in vitro. Autoradiography was used to determine changes in the thymidine index of the tumor under the influence of different intensities of SMF.

In addition, we tested SMF as an enhancer of the efficacy of chemotherapy to depress DNA synthesis of human glioma in vitro. We obtained the first encouraging results, which confirm that SMF have a direct influence on depression of in vitro growth of glial tumors and enhance the effects of cytostatic agents. The positive results of these studies can be used in neurosurgical practice for administration of combined individual therapy to neurooncological patients.

Heretofore, only surgery, chemotherapy and radiation had been used in neurosurgery; however, the trauma and hazard of surgical intervention, as well as inadequacy of the effects of chemotherapy, make it urgent to search for new methods of treatment.

In recent years, magnetotherapy has gained a place in combined therapy. At the present time, all cases where surgical management is contraindicated (presence of intercurrent disease, advanced age of patients) are indications for the use of guided MF for vascular aneurysms of the brain. Aneurysmal thrombus formation under the influence of SMF yielded results that were not inferior to surgical management. Magnetic cuffs are indicated in cases where endovascular surgery is contraindicated (presence of concomitant disease, severe patient reaction to the Matasa test and others).

The feasibility of magnetobiological treatment of neurooncological diseases is determined on the basis of the condition of the hemopoietic system, changes in neuropsychological state, tests of individual sensitivity of tumor tissue to VMF, which is determined in vitro.

Adverse effects are seldom observed with MF, as compared to ionizing radiation.

Thus, there are few absolute contraindications to magnetotherapy. Hypocoagulation of blood and recurrent stress reactions with the use of MF of different parameters, as well as individual sensitivity to this factor, are among the relative contraindications that should be considered.

PHOTO CAPTIONS

2. p 19. Stereotactic electromagnetic unit. a) outside view; b) control console.

3. p 20. Angiogram of patients with aneurysm of anterior communicating artery. Top--before thrombus formation, bottom--after.

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CHANGES IN PERIPHERAL CIRCULATION OF LIMBS DURING BONE REGENERATION UNDER INFLUENCE OF LOW-FREQUENCY MAGNETIC FIELDS

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 (manuscript received 27 Feb 81) pp 24-27

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[Text] Reparative regenerative processes in bone tissue are largely determined by the state of circulation in the injured limb segment.

Our objective here was to investigate the role of peripheral circulation in the extremity in the mechanism of action of low-frequency magnetic fields (MF)--variable MF (VMF)--on reparative regeneration of bone. This work consists of two parts, experimental and clinical.

A Polyus-1 type unit was used for both experimental and clinical use of MF. The MF generated by this unit is of a low frequency (50 Hz, 10 mT induction) and it operates in a continuous mode. The inductors, which are the working part of the instrument, consist of 2 parallelepipeds with 50×50 mm area at the ends and 150 mm in length.

We used 125 mature rabbits in the experiments. A subperiosteal defect 4 mm in size was produced in the middle third of the radius of all animals. The limb was not immobilized since there is virtually no movement between the ulna and radius under normal conditions by virtue of very sturdy syndesmosis. The injured limb of 71 rabbits was exposed to VMF. Both inductors were placed transversely right on the region of the defect. Treatments were for 20 min a day, daily to a total of 14. Simulation of the effects of VMF was used on the 54 rabbits of the control group.

To examine peripheral circulation and monitor bone regeneration, we used clinical observation, roentgenological and morphological examinations, polarographic determination of oxygen tension (pO_2) in muscles of the injured and intact legs using an LP-7 polarograph.

The vessels were filled with a mixture of India ink and gelatin according to G. A. Onopriyenko to examine the vascular net in the region of the fracture, after which we prepared histological preparations. For quantitative analysis of the vascular network in cleared preparations, we used the method of television planimetry (V. D. Manyakhin; I. M. Mitbreyt et al.), which was performed in the Cytospectrophotometry Laboratory of the Second Moscow Medical Institute imeni N. I. Pirogov together with L. Ye. Nemirovskiy and I. G. Suvorova. Hard open platinum electrodes were used to measure pO_2 and calomel electrodes for comparison. The mode of powering the electrodes was chronoamperometric; maximum voltage was recorded in a pulsed polarization mode (V. A. Dirin).

Microscopy of the fracture region revealed distinct differences in time of formation of regenerated bone between the experimental and control groups of animals. In addition, there was more intensive development of the vascular network in the region of the fracture in rabbits treated with VMF. The morphological difference between the experimental and control group began to be evident in the 1st week after surgery, but it was the most marked by the 14th-21st day of reparative regeneration. Thus, by the 21st day, at the site of the radial defect of animals in the experimental group, a bone regenerate with small layers of cartilaginous tissue was demonstrable. There were many vessels in the intertrabecular spaces of spongy bone tissue of the regenerated bone. In the control group, vascular cartilaginous tissue occupied most of the regenerated bone and cartilage. According to the results of television planimetry, the area of vessels in the fracture regions was larger in experimental animals than in the control (Figure 1): 44±2.3 and 37.4±2.6 AU [arbitrary units], respectively ($P<0.01$). In the other parts of the injury region, the area of vessels was also considerably larger in the experimental group. After 30 days, this group presented a bone regenerate at the site of the former radial defect, with signs of formation of cortical layer and medullary canal; in the control group the defect was filled with immature osseous and cartilaginous tissue. Television planimetry showed that the area of bone regenerate vessels was larger in experimental animals than in the control (51.4±1.7 and 46.0±2.1 AU, respectively; $P<0.05$). By the 75th postoperative day, there was restoration not only of integrity but structure of the radius in the experimental group. The bone regenerate that filled the defect acquired the typical structure of a long bone diaphysis; in the control group it consisted of spongy osseous tissue, which is not inherent in structure of the diaphysis. The area of vessels in the region of formation of regenerate was insignificantly larger in the experimental group than the control, but the difference was unreliable: $P>0.05$ (see Figure 1).

Polarographic studies revealed that the base pO_2 in limb muscles constituted 25.75±2.4 mm Hg, with appreciable drop on the 2d postoperative day (to 7.48±0.78 mm Hg), whereas in the intact limb there was insignificant elevation (to 29.16±0.9 mm Hg), as compared to the base level. There was gradual rise of pO_2 in muscles of the injured extremity in the course of reparative regeneration, and this was related to the degree of normalization of circulation in the fracture region, which is consistent with morphological findings. In the experimental group there was considerably faster normalization of pO_2

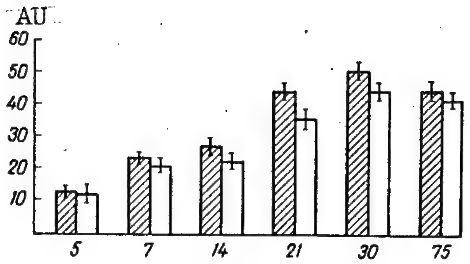

Figure 1.
Dynamics of changes in area of vessels in defect of rabbit radius in the course of regeneration with and without exposure to VMF (according to results of television planimetry). Here and in Figure 2:
X-axis, post-trauma days
Light columns--control;
striped--experiment

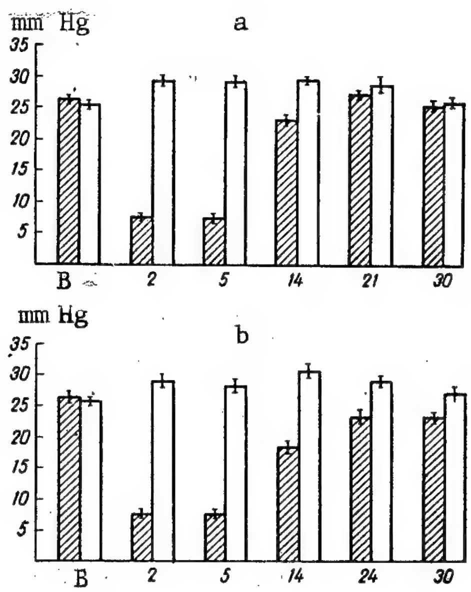

Figure 2.
Dynamics of pO_2 changes in muscles of injured (striped columns) and intact (white columns) limbs of animals in the course of reparative bone regeneration.
a) experiment (VMF)
b) control (without VMF)
B) base state

in the injured extremity than in the control (Figure 2): by the 30th postoperative day, pO_2 of muscles of the injured limb of the experimental group did not differ from that of the intact extremity; at the same time, the difference persisted in the control group (see Figure 2), which is indicative of elimination of trophic disturbances and normalization of energy supply to tissues in the region of the fracture under the influence of VMF.

Clinical observation revealed earlier disappearance of edema in the injured limb, formation of a finer cutaneous cicatrix and earlier use of the limb in the experimental group. Roentgenological examination revealed that processes of consolidation of the radius occurred sooner in experimental animals than the control, they were more marked and terminated much faster. Total restoration of the shape of the bone occurred by the 75th day in the experimental group, whereas in the control group there were no medullary canal or cortical elements in the region of the defect at this time.

The clinical part of this study consists of observation of 103 patients with fractures of the distal epimetaphysis of the radius.

Union of fractures was checked by clinical tests, functional examination of peripheral circulation, as well as roentgenology.

Examination of peripheral circulation in the limbs involved electrothermometry of digital skin, rheovasography and measurement of intraosseous blood pressure (IBP). From the rheovasographic data, using the formula of Nyboer, we calculated minute volume of circulation (MV), and from the synchronous tracing of the EKG and rheovasograms we determined the rate of pulse wave propagation (RPWP), which characterizes the tonus of great vessels.

The main group (with VMF treatments starting on second day after trauma, along with other therapy of the fracture) consisted of 68 patients and the control, 35 patients.

VMF treatment was prescribed daily, for 20 min at a time, to a total of 14 treatments. The equipment operating mode and characteristics of MF used for treatment were the same as in the experimental studies. The injured arm in a plaster cast was placed between the end surfaces of the inductors in such a manner that the fracture region was in contact with them. We performed manual reposition under local anesthesia, with immobilization in a partial ["dorsal"] plaster cast on all patients with fractures of the distal epimetaphysis of the radius with displacement of bone fragments.

We assessed the results of treatment according to anatomical, roentgenological and functional parameters of the injured limb 2 weeks after removing the cast.

Examination of peripheral circulation revealed that it differed significantly in the extremity with fracture of distal epimetaphysis of the radius with displacement of fragments from circulation in the intact limb. The differences consisted of decreased filling of the injured arm (according to MV data), increased tonus of great vessels (according to RPWP), intensification of circulation in cutaneous vessels (according to electrothermometry) and worsening of intraosseous circulation (according to IBP). Thus, in the main group, MV of the injured and intact limbs constituted 2.44 ± 0.104 mℓ/cm^3 and 3.04 ± 0.81 mℓ/cm^3 tissue/min, respectively ($P<0.001$), RPWP constituted 11.87 ± 0.206 and 10.566 ± 0.174 m/s ($P<0.001$). Cutaneous temperature was elevated by 1.2°C. IBP was quite low (25.18 ± 0.87 mm water column) in the injured limb, whereas it was 68.68 ± 3.18 mm water ($P<0.001$) in the intact one. We failed to demonstrate reliable differences in the above indicators of peripheral circulation between the main and control groups on the day trauma was sustained.

Starting on the 21st day of regeneration, there were significant differences between circulation in the injured limb of patients in the main and control groups. Thus, MV constituted 2.78 ± 0.08 and 2.45 ± 0.115 mℓ/100 cm^3 tissue/min ($P<0.01$), respectively, 21 days after trauma in the injured limb. Tonus of great vessels of the injured limb was low in the main group, as compared to the control: RPWR constituted 10.293 ± 0.146 and 10.808 ± 0.172 m/s, respectively ($P<0.001$). Skin temperature on the side of the injury was 0.7°C elevated in the main group, whereas in the control group temperature asymmetry constituted 1°C; IBP was considerably higher on the injured side in the main group than the control, constituting 64.0 ± 2.36 mm water ($P<0.001$).

These data are indicative of the active nature of increase in intensity of circulation in the injured limb under the influence of VMF.

On the day that the cast was removed, according to all tested parameters circulation in the injured extremity of patients in the main group did not differ from that of the intact limb, whereas in the control group considerable differences between the two limbs were noted.

The results of functional examination of peripheral circulation conformed well with the results of clinical and roentgenological studies. According to the clinical data, patients receiving VMF treatment showed faster disappearance of pain and edema of fingers on the injured side; on the day their cast was removed, there was insignificant edema in the region of the wrist, with no pain in the region of the fracture. In the rehabilitation period, movements in the wrist and pronation-supination of the arm were restored sooner than in the control group of patients.

As a result, 2 weeks after removal of the cast, the amplitude of movements of the injured arm was considerably broader in the main group than the control. The faster restoration of function of the injured extremity under the influence of VMF resulted in shortening the period of temporary disability by an average of 9 days in the main group of patients.

Thus, our data indicate that MF at a frequency of 50 Hz and induction of 10 mT under both experimental and clinical conditions have a marked effect on peripheral circulation in extremities and improve tissular trophics in the course of bone regeneration in patients with fracture of the distal epimetaphysis of the radius.

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CHANGES IN TRANSCAPILLARY METABOLISM IN PATIENTS WITH CHRONIC VENOUS INSUFFICIENCY OF LEGS UNDER INFLUENCE OF STATIC MAGNETIC FIELDS

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY in Russian No 4, Jul-Aug 81 (manuscript received 13 Feb 81) pp 28-31

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[Text] Much attention is devoted in modern surgery to diagnosis and treatment of peripheral vascular diseases. Among them, acute thrombosis, varicose and postthrombophlebitic diseases occupy a considerable place. The existing methods of treating these diseases do not always yield the desired results.

In recent years, magnetotherapy has gained popularity in clinical practice. The experimental and clinical data that have been accumulated are indicative of the beneficial effects of magnetic fields (MF) on some forms of vascular pathology (M. F. Murav'yev et al.; A. M. Demetskiy et al.; B. N. Zhukov et al., 1977, 1979; R. P. Kikut, and others). However, the mechanism of therapeutic action of MF, indications and contraindications for use thereof have not been sufficiently investigated.

For this reason, we studied transcapillary metabolism and microcirculation in patients with chronic venous insufficiency of the legs. In accordance with our objectives, we monitored dynamically a number of biophysical and physiological parameters using the following methods.

Oxygen tension (pO_2) was measured by polarography using M-95 and ON-102 instruments in arterial and venous blood, and tissues. The redox potential was measured with redox-metric sensors on a millivoltmeter in blood, plasma and tissues. Oxygenation of hemoglobin was estimated from the readings of an 057 type oxyhemometer in arterial and venous blood. Capillary filtrate and protein loss were determined by the venous-venous gradient method that we proposed earlier (B. N. Zhukov et al., 1977). Concentration of sodium ions in venous blood plasma was assayed by spectrography.

Concurrently, we monitored microcirculatory processes by radionuclide diagnostic methods, intravital microscopy, "termovideniye"

["thermovision"--scan thermography?], examination of hemostatic factors, etc. Hemodynamic parameters were assessed according to results of polyrheovasography, radiodiagnostic methods, contrast phleboscopy and phlebography.

In this report we shall discuss data on the effects of a static magnetic field (SMF) of low induction (from 2.5 to 10 mT) generated by a YeYa unit (VDNKh [Exhibition of Achievements of the National Economy of the USSR] catalogue, 1979, code IX 7130). We determined duration of exposure and induction of SMF in accordance with the nature of the pathological process and individual distinctions of patients. The target was placed in a solenoid with a diameter of 63 cm longitudinally to the direction of SMF lines of force.

Patients with varicose and postthrombophlebitic diseases of veins of the legs were characterized by the clinical syndrome of chronic venous insufficiency, manifested by pain and edema varying in intensity, trophic disorders of soft tissues in the distal parts of the legs and capillary cellulitis, dermatitis, eczema and trophic ulcers. The severity of these manifestations increased with increase in duration of disease and degree of suprafascial venous hypertension.

We had 132 patients under observation, who were divided into 2 groups. The first consisted of 54 patients with varicose disease of the legs at the stage of compensation and decompensation; they ranged in age from 18 to 66 years and illness was of 3 to 13 years duration; the second group consisted of 78 people with postthrombophlebitic disease (varicose and edematous forms) ranging in age from 24 to 68 years, with 2 to 40 years duration of illness.

Table 1 shows that there was no impairment of either colloid-osmotic parameters of transcapillary metabolism nor oxygenation of tissues in the first group of patients at the compensation stage. We found (Table 2) an increase in oxyhemoglobin content of venous blood and drop of tissular pO_2, which could serve as confirmation of arteriovenous shunts in microcirculatory zones.

Table 1. Effect of magnetotherapy on transcapillary metabolism of patients with varicose and postthrombophlebitic diseases of the legs (M±m)

Leg disease	Capillary filtrate, mℓ		Protein loss, %		Sodium concentration, mM/ℓ	
	before	after	before	after	before	after
	treatment		treatment		treatment	
Varicose veins (1st group):						
compensation stage	2,12±1,04	1,20±0,7	0,08±0,001	0,03±0,002	146,4±16,4	147,2±10,4
decompensation stage	5,25±1,3	3,93±1,2	0,27±0,01	0,15±0,03	145,8±12,2	146,1±12,6
Postthrombophlebitic disease (2d group):						
varicose form	5,24±1,3	4,21±0,23	0,24±0,01	0,17±0,02	146,6±18,2	147,5±12,4
edematous form	12,64±2,1	6,83±1,23	0,62±0,02	0,21±0,03	139,6±14,3	147±12,2

Table 2. Oxygenation in patients with varicose and postthrombophlebitic diseases of legs before and after SMF treatment (M±m)

Disease	Parameter	Arm (control)	Involved leg before treatment	Involved leg after treatment
Varicose disease at decompensation stage	pO_2, mm Hg:			
	arterial blood	116±2,1	106±1,2	92±1,8
	venous blood	60±1,5	60±2,6	59±4,4
	tissue	42±0,8	21±1,8	30±1,6
	Oxygenation of hemoglobin, %:			
	arterial blood	91±3,2	91±1,8	90±1,2
	venous blood	42±3,4	70±1,8	64±0,8
	Redox potential, mV:			
	blood	102±6,6	135±7,5	141±1,8
	plasma	24±1,7	24±1,8	35±2,4
	tissue	—42±1,8	—68±2,3	—61±1,6
Postthrombophlebitic disease, edematous form	pO_2, mm Hg:			
	arterial blood	116±2,1	98±2,8	108±1,6
	venous blood	60±1,5	75±1,4	62±1,8
	tissue	42±0,8	12±0,6	18±0,4
	Oxygenation of hemoglobin, %:			
	arterial blood	91±3,2	94±0,5	96±0,8
	venous blood	42±3,4	50±2,3	39±1,9
	Redox potential, mV:			
	blood	102±6,6	132±8,2	160±5,0
	plasma	24±1,7	29±1,8	40±2,2
	tissue	—42±1,8	—124±4,3	—88±2,6

There was a corresponding decrease in redox potential of extracellular volume and increase in amount of capillary filtrate, which was indicative of a tendency toward migration of liquid part of blood into interstitial tissue. Use of SMF caused dilatation of capacitive vessels, undesirable arteriovenous shunting and increase in venous deposition of blood. The change in transcapillary metabolism and redox processes does not lead to a beneficial effect. For this reason, we believe that it is undesirable to use magnetotherapy for varicose veins and surgery should be considered the chief method for correcting transcapillary metabolism in the presence of this disease.

In the second group of patients there were insignificant changes in transcapillary metabolism under the influence of SMF (see Table 1). With the varicose form of postthrombophlebitic disease, SMF caused deposition of venous blood and intensification of tissular edema. There is much better correction of hemodynamic disturbances by surgical management.

The changes in transcapillary metabolism of patients with the edematous form of postthrombophlebitic disease are attributable to impaired correlations

between hydrostatic and colloid-osmotic pressure. Thus, there is an increase in amount of capillary filtrate, increased protein loss, decrease in sodium ion content of venous blood in the involved leg. As a consequence, filtration pressure rises and there is development of interstitial edema and tissular hypoxia. In the extracellular part of the microcirculation there is accumulation of incompletely oxidized products which have a secondary deleterious effect on tissue and the vascular wall, as indicated by changes in redox potential in blood, plasma and tissues (see Table 2). The increase in oxyhemoglobin of venous blood, which is also observed, is the result of arteriovenous shunting.

In this group of patients, the amount of capillary filtrate decreased, as did protein loss, and there was an increase in sodium concentration in venous blood, which was indicative of activation of the sodium pump of tissues, under the influence of SMF. Sodium ions entering into the blood stream cause fluid to migrate from interstitial tissue into blood. Thus, we observed quantitative stabilization of protein and normalization of colloid-osmotic pressure, which aids in causing edema to disappear, in the microcirculatory bed under the influence of SMF.

In addition, there was significant change in tissue metabolism, as indicated by the reliable decrease in oxyhemoglobin content of venous blood. The latter occurs as a result of improvement of microcirculatory processes (results of intravital microscopy) and increased oxygen utilization in aerobic metabolic processes in tissues.

Thus, SMF are instrumental in significant improvement of transcapillary metabolism in patients with the edematous form of postthrombophlebitic disease, causing a dehydrating effect and appreciably improving the oxygen-transport function of the microvascular system. Rheopolyglucin, solkoseril, trental and other products that improve microcirculation have a more marked therapeutic effect with the use of SMF. "Thermovision" can be used to monitor efficacy of therapy.

Conclusions

1. Chronic venous insufficiency of the legs is characterized by changes in transcapillary metabolism and microcirculatory processes, in addition to hemodynamic disturbances.

2. A static magnetic field (SMF) of low intensity (2.5-10 mT) is one of the effective physiotherapeutic factors used in phlebological practice.

3. SMF improves considerably transcapillary metabolism, has a dehydrating effect due to elevation of colloid-osmotic pressure in the microvascular system and activation of the sodium pump, enhances oxygen transport and utilization in tissues in patients with the edematous form of postthrombophlebitic disease. SMF does not elicit a marked therapeutic response in patients with the varicose form of chronic venous insufficiency, and use thereof is not warranted.

4. Objective evaluation of hemodynamic parameters and microcirculatory processes facilitates differentiated use of SMF for patients with pathology of peripheral vessels.

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CHROMATIN OF RAT BRAIN NEURONS AND NUCLEIC ACIDS OF MUSCLES AS RELATED TO LOCALIZATION OF DECIMETER WAVES DURING EXERCISE

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[Text] In recent years, physical factors, in particular waves in the decimeter range (DMW) have been used to restore work capacity of athletes after intensive training (N. A. Zagorskaya and others). It is imperative to investigate the mechanism of DMW effects during physical exercise.

Our objective here was to make an experimental study of the effects of different localizations of DMW on structural and functional state of chromatin (deoxyribonucleoprotein--DNP) of cerebral neuronal nuclei and nucleic acid content of rat muscles during intensive physical exercise.

Experiments were conducted on 60 white male Wistar rats weighing 180-220 g. The physical load consisted of graded daily swimming in fresh water at a temperature of 28-32° for 4 weeks using a previously described method (Z. A. Sokolova and L. V. Mikhaylik). DMW were generated by a Volna-1 unit (emitter with 4 cm diameter, intensity of 120 mW/cm^2). The waves were delivered to the region of the femoral muscles, adrenals or head for 3 min/day to a total of 10 times.

Nucleic acid content of skeletal muscles was assayed by the two-wave spectrophotometric method of R. G. Tsanev and G. G. Markov; structural and functional state of DNP in cerebral neuronal nuclei was examined by the microfluorometric method of Rigler, which is based on measurement of intensity of secondary fluorescence of the chromatin DNA--fluorescent acridine orange complex at a wavelength of 530 nm using an MSP-0.5 Opton (FRG) fluorescence microscope. We examined the large pyramidal neurons of the fifth layer, stellate neurons of the fourth layer and glial cells (both satellites of large layer V pyramidal neurons and free forms) in the sensorimotor cortex of the brain. To identify the zones we used the classification of V. M.

Svetukhina. In the hippocampus, we examined large pyramidal neurons of field CA_3 and granular neurons of the dentate gyrus. We previously described the technique for treatment of brain tissue (Z. A. Sokolova).

The results of assaying nucleic acids in rat skeletal muscles during exercise and with different localizations of DMW are listed in Table 1. Physical exercise led to statistically reliable decrease in RNA content of muscles and did not affect the quantity of DNA. With exposure of the region of the femoral muscles to DMW, there was reliable elevation of RNA level to normal, while DNA content did not change. Delivery of DMW to the adrenal or head region did not elicit changes in nucleic acid content of muscles and RNA level remained low, like the control group of animals.

Table 1. Nucleic acid content of rat skeletal muscles under different experimental conditions (in mg% phosphorus in dry tissue mass; M±m)

Experimental conditions	RNA	DNA
Normal	46,3±1,41	22,2±1,29
Exercise	38,6±0,83	22,3±1,34
P	<0,001	>0,5
Exercise + DMW to femoral muscles	45,2±2,12	23,2±1,29
P	<0,01	>0,5
Exercise + DMW to adrenal region	36,2±1,85	20,7±0,87
P	>0,25	>0,25
Exercise + DMW to head region	32,7±2,63	19,3±1,45
P	>0,1	>0,25

Table 2 shows that exercise did not affect intensity of fluorescence of neurons from the examined brain formations; however, it elicited an appreciable decline of this parameter in nuclei of oligodendrogliocytes--satellites of large pyramidal neurons of the cerebral cortex. Exposure of femoral muscles of rats submitted to intensive exercise to DMW did not alter the intensity of fluorescence of DNP of nuclei of neurons and glia of the cerebral cortex and hippocampus. With delivery of DMW to the adrenal region there was statistically reliable increase in adsorption of acridine orange by the nuclei of the large pyramidal neurons of the sensorimotor region of the cerebral cortex. In other types of neurons examined this parameter did not change. The most significant changes were demonstrable with exposure of DMW to the head of rats submitted to exercise. Among the types of nerve cells studied, the most "responsive" to DMW were the nuclei of large pyramidal neurons of the cerebral cortex and hippocampus, as had been previously observed (O. A. Krylov et al.).

Thus, DMW had different effects on plastic properties of muscle tissue and structural-functional state of chromatin DNA of rat brain neurons during intensive exercise, depending on the area exposed to them. Delivery of DMW to the region of the femoral muscles did not alter the chromatin of cerebral neurons, but did lead to elevation of RNA level in muscle tissue, thereby

Table 2. Intensity of fluorescence of nuclear DNP of neurons and neuroglia of sensorimotor cortex and hippocampus of rats under different experimental conditions (% of data obtained during exercise; M±m)

Experimental conditions	Cerebral cortex				Hippocampus	
	large pyramidal neurons	stellate neurons	oligodendrogliocytes: satellites of large pyramidal neurons	oligodendrogliocytes: "free" forms	large pyramidal neurons	granular neurons of dentate gyrus
Normal	112,8±10,8	115,9±7,7	146,7±7,6	119,2±5,4	82,2±7,0	105,6±13,3
Exercise	100,0±11,8	100,0±8,1	100,0±6,7	100,0±7,3	100,0±9,8	100,0±10,1
P	>0,5	>0,25	<0,001	>0,05	>0,1	>0,5
Exercise + DMW to femoral muscles	87,4±8,7	84,8±5,9	80,5±8,8	82,5±6,8	94,0±9,0	82,6±7,7
P	>0,1	>0,1	>0,05	>0,05	>0,5	>0,05
Exercise + DMW to adrenal region	149,7±11,1	111,2±10,8	—	—	—	117,0±11,4
P	<0,002	>0,25				>0,5
Exercise + DMW to head region	222,8±16,9	118,9±13,9	100,0±6,8	129,4±13,2	189,0±15,6	146,5±16,8
P	<0,01	>0,25	>0,5	>0,05	<0,01	>0,05

eliminating the adverse changes in nucleic acid metabolism that occurred during exercise. This effect could be related to the fact that, under the influence of DMW, conditions are created in tissues for improvement of circulation and increase in biosynthetic processes (M. A. Shishlo and Yu. N. Korolev).

Exposure of the adrenal and head region to DMW while rats were exercising, on the contrary, failed to affect plastic metabolism in muscles, but increased fluorescence of chromatin DNA of large pyramidal neurons of the sensorimotor cortex and hippocampus. These changes can be interpreted as activation of the genetic system of neurons, since the increase in adsorption of acridine orange is indicative of increase in number of DNA segments free of protein and, consequently, increase in its matrix activity (Rigler et al.).

Our experimental findings on the effects of DMW delivered to different regions warrant the conclusion that, from the standpoint of normalizing impaired nucleic metabolism in muscles, their direct effect on muscular fatigue is the most desirable during intensive exercise. In those cases where exercise is related more to tension of the nervous system than muscular fatigue, it is apparently preferable to use DMW to the adrenal or head region. However, the latter localization of exposure requires investigation with regard to a number of other biochemical and physiological parameters.

Conclusions

1. Exposure of the rat femoral muscles to DMW caused elevation of RNA level in tired muscles, which had been low as a result of intensive exercise, but had no effect on structural and functional state of chromatin DNA of cerebral neurons.

2. Exposure of rat adrenal region to DMW during exercise increased fluorescence of chromatin DNA of nuclei of large pyramidal neurons in the sensorimotor cortex and had no effect on nucleic acid level in skeletal muscles.

3. Exposure of the rat's head to DMW during exercise led to increased adsorption of acridine orange by the nuclei of large pyramidal neurons, not only in the sensorimotor cortex, but hippocampus; this was not associated with change in nucleic acid content of muscles.

4. The localization of DMW determines the direction of changes in physicochemical state of nuclear DNP of cerebral neurons and nucleic acid content of rat muscles during intensive physical exercise.

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DISTRIBUTION OF HEAT IN BIOLOGICAL TISSUES UNDER INFLUENCE OF UHF ELECTROMAGNETIC FIELDS

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[Article by P.V. Svetitskiy, Uzbek Scientific Research Institute of Oncology and Radiology, Tashkent]

[Text] Use of ultrahigh-frequency electromagnetic fields (UHF EMF) in experimental oncology and, in particular, in combination with radiation therapy showed it to be effective in treatment of experimental tumors (M. G. Panin and A. P. Panina; V. F. Lopatin; Dietzel et al.; K. Overgaard and I. Overgaard). Preliminary observations of use of UHF EMF in thermogenic modes on patients with tumors of the head and neck revealed that they do not elicit serious complications and are well tolerated by patients (P. V. Svetitskiy; P. V. Svetitskiy and N. S. Yadgarova).

In practical work, one must have knowledge about the link between nature of distribution of generated heat in biological tissues and technical parameters in order to control the biological effects of UHF EMF hyperthermia.

The same intensity of exogenous EMF can elicit different levels of induced endogenous EMF, for which reason there is a change in heating of tissues.

This phenomenon depends on the size and shape of biological objects, their orientation in relation to EMF vectors, morphological structures and electric properties of tissues, intensity of energy emission by tissues as a result of vital functions, as well as several other, as yet little-studied factors (V. M. Shtemler and S. V. Kolesnikov). For this reason, we conducted experimental studies to determine the distribution of heat in biological tissues exposed to UHF radiation, which could serve as a guide for clinical work.

Material and Methods

Studies were conducted on 5 mongrel dogs weighing up to 30 kg. We examined their thigh, which has the largest volume (up to 50 mm in thickness) and relatively homogeneous (muscular) structure, so that we could standardize the experiment.

Temperature distribution (°C) in biological tissue sections under the influence of UHF radiation

Section depth, mm	Distance from edge of electrode, mm: 0	10	20	30	40	50
	Electrodes 15 mm in diameter					
0	41,5	36,5	36,5	36,5	36,5	36,5
10	41,3	38,0	36,7	36,5		
20	40,5	38,0	36,7	36,5		
25	40,0	37,5	36,7	36,5		
	Electrodes 20 mm in diameter					
0	41,5	36,5	36,5	36,5	36,5	36,5
10	41,0	40,5	37,5	36,5		
20	40,3	40,3	37,0	36,5		
25	40,0	37,5	36,0	36,5		
	Electrodes 25 mm in diameter					
0	41,5	36,5	36,5	36,5	36,5	36,5
10	41,0	39,0	36,5	36,5		
20	40,3	39,0	38,0	36,8	36,5	
25	40,0	38,5	37,5	37,0	36,5	
	Electrodes 40 mm in diameter					
0	41,5	36,5	36,5	36,5	36,5	36,5
10	40,8	39,0	38,0	36,5		
20	40,2	38,5	37,6	37,0	36,5	
25	40,0	38,3	37,4	37,2	37,0	36,5

The animals were immobilized on their backs under hexenal anesthesia. The tested limb was additionally secured. The integument was surgically removed from the thigh. Equal-sized electrodes of the UHF emitter were secured to the anterior and posterior surfaces in the middle of the thigh. In each individual case, we used electrodes with 15, 20, 25 and 40 mm diameters, with fixed dielectric (plexiglas) 10 mm in thickness. The dimensions of the dielectrics corresponded to those of the electrodes. The presence of dielectrics provided a stationary space between the object and electrodes.

In order to obtain more accurate heat control in the tested points of the biological object, we used the afterloading method. Thigh tissues distal to the edge of the electrodes were pierced with a thick puncture needle every 10 mm. Cellophane tubes, 1.5 mm in diameter and 5 mm in length, were inserted in the formed orifices.

The presence of formed "gates" provided for accuracy and speed of measurement of temperature made by the probes of copper-constantan thermocouples. The temperature on the surface of the biological object was taken every 10 min in the proximal part of the extremity.

The tissues were heated by exposure to UHF radiation at 40 W. The temperature of tissues under the electrodes was brought to 40-42°C (the initial temperature of the muscles being 36.5°C).

In view of the thermal inertia of the tested tissues, we checked the temperature at the maximum permissible intervals (up to 3-4 s) with the UHF emitter turned off. Of course, under such conditions there were difficulties in assuring accuracy of measurements (error factor of up to +0.5°C).

However, the obtained data can be used to solve the problem set forth, by making certain assumptions. In order to define the quantitative temperature changes in depth and on the surface of the heated tissues, as well as to determine isometric surfaces in depth and distribution of isotherms in sections, the obtained experimental data were submitted to mathematical analysis, which was based on the theses of analytical geometry (I. I. Privalov; G. Korn and T. Korn; N. Bailey).

Results and Discussion

Our results revealed that there were certain patterns in the distribution of temperatures in sections of biological tissues under the influence of UHF radiation (see Table).

Uniform heating of tissue with stabilization of temperatures occurred 2-3 min after the start of the hyperthermia session. Upon termination of heating, the temperature reverted to normal (equal to temperature of surrounding tissues) 5-7 min after the UHF unit was turned off, which coincides with the data of K. Overgaard and I. Overgaard et al., who made experimental studies of healthy and tumor tissues to determine the properties of distribution of UHF EMF.

As can be seen in the table, the superficial temperature of the heated object constituted 41.5°C at the edge of the electrode, regardless of its diameter, whereas at a distance of 100 mm it became equal to body temperature (36.5°C).

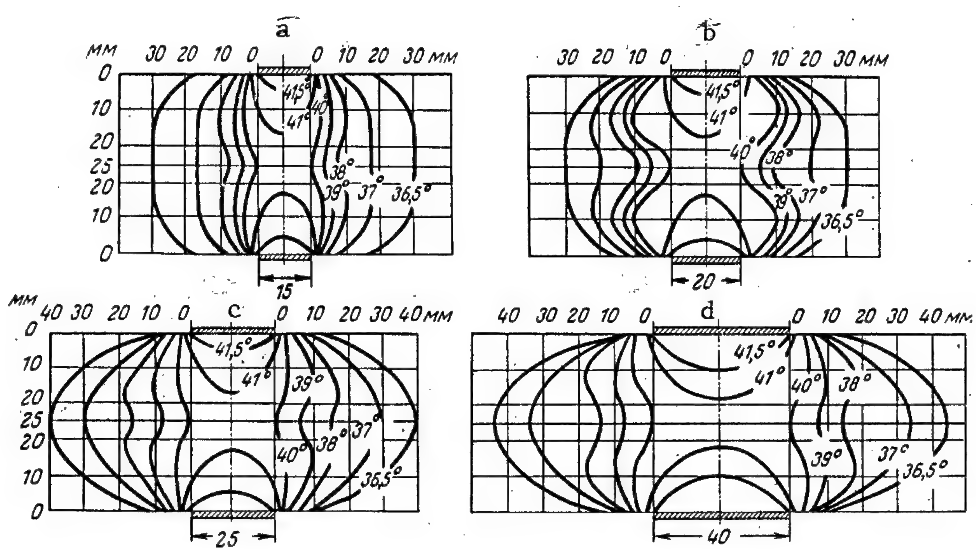

Figure 1. Isotherms in biological object under the influence of UHF hyperthermia with electrodes 15 mm (a), 20 mm (b), 25 mm (c) and 40 mm (d) in diameter. X-axis, distance from edge of electrode on tissue surface; y-axis, section in depth.

With electrodes 15 mm in diameter, the temperature of tissues 10 mm in depth along the edge of the electrode reached 41.3°C, whereas at distances of 10, 20 and 30 mm along the edge it dropped to 38, 36.7 and 36.5°C, respectively. At depths of 20 and 25 mm in the same projections, the temperatures were 40.5, 38, 36.7, 36.5°C and 40, 37.5, 36.7 and 36.5°C, respectively.

With electrodes 20 mm in diameter, at the above depths and areas, the tissues heated up to 41, 40.5, 37.5, 36.5, 40.3, 40.3, 37, 36.5, 40, 37.5, 36.5 and 36.5°C.

Use of electrodes 25 mm in diameter in the same projections heated tissues to 41, 39, 36.5, 36.5, 40.3, 39, 38, 36.8 and 36.5°C, and at a distance of 40 mm from the edge of the electrode to 40, 38.5, 37.5, 37 and 36.5°C.

Heating tissues with electrodes 40 mm in diameter was associated with the following distribution of temperatures in examined tissues: 40.8, 39, 38, 36.5, 40.2, 38.5, 37.6, 37, 36.5, 40, 38.3, 37.4, 37.2 and 37°C: at 50 mm away from the edge of the electrode the temperature equaled that of surrounding tissues.

Isotherms were plotted on the surface and in depth of tissues for each of the four electrodes on the basis of the obtained results (Figure 1).

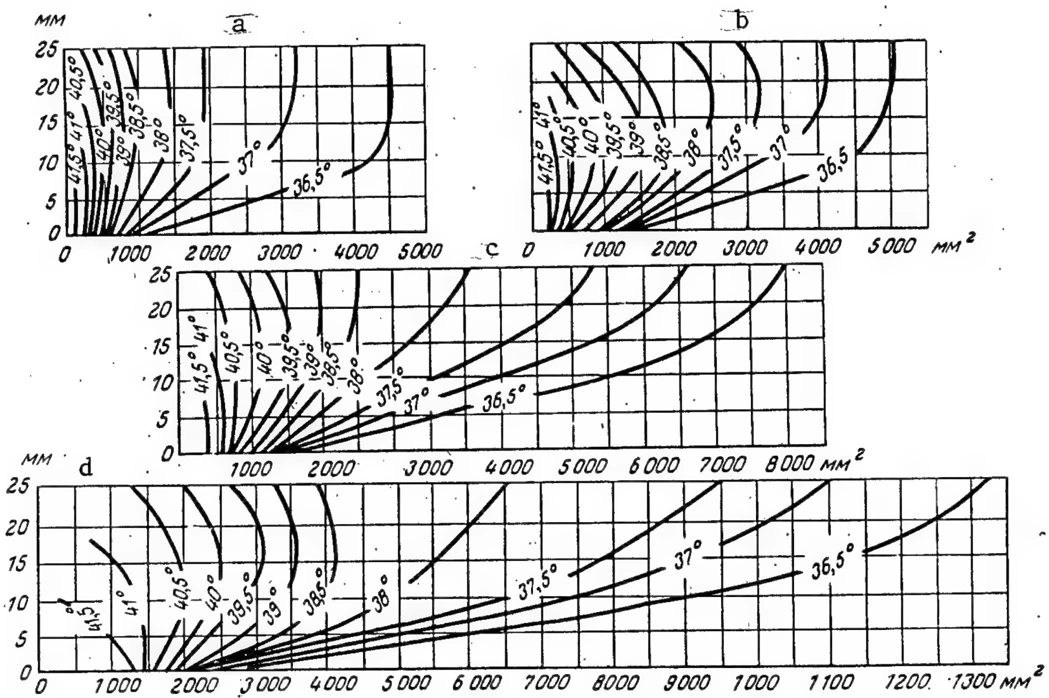

Figure 2. Charts of relationship of heat distribution in biological object combining tissue temperature, isotherm area and depth of section for UHF emitter electrodes 15, 20, 25 and 40 mm in diameter (a, b, c and d, respectively). X-axis, isotherm areas all of which increase; y-axis, section depth.

It was found that isotherms of 36.5°C, which separate heated tissue from the rest in cross sections in depth, are circumferences describing a three-dimensional figure similar to a spheroid truncated at the apices (at contacts with electrodes).

The nature of distribution of isotherms within the spheroid resembles the known system of distribution of voltage of a UHF electric field (N. M. Liventsov). As can be seen in Figure 1, the isotherms are symmetrical in relation to the electrode axis. Thus, in deep tissue, isotherms 41.5 and 41°C are situated under the electrodes. Isotherms 40, 39 and 38°C are convoluted (convex at a depth of 10 mm and concave at depths of 20 and 25 mm).

Isotherms 37 and 36.5°C (with the exception of b) circumscribe a spheroid smoothly.

These isotherm maps enabled us to define the isotherm circumferences and isotherm areas of circumferences in sections of spheroids, on the basis of which relationship graphs were plotted (Figure 2), which unite tissue temperature, isotherm areas and section depths in planes that are parallel to electrodes of different diameters. The isotherms from 36.5 to 41.5° are illustrated on the field of the graphs. These graphs are intended for practical work to determine an unknown parameter on the basis of two known ones.

For example, one needs to determine the isotherm area (F, mm^2) at a section depth of 10 mm, tissue temperature in the range of 39-40° and with electrodes 15 mm in diameter.

To solve this problem on the relationship graph (see Figure 2a), we find the isotherm areas corresponding to 500 and 800 mm^2 in the section at a depth of 10 mm at intersections with isotherms 40 and 39°C on the F scale. Consequently, in the given range of temperatures, the isotherm area will be: $800 - 500 = 300$ mm^2. Other unknown parameters are found similarly.

Thus, our results enabled us to determine some of the correlations between external parameters of UHF radiation and formed distribution of heat in heated tissues. These data characterize the phenomena studied with some degree of accuracy, and they can be used in practical work.

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EFFECTS OF LOW-FREQUENCY (50 Hz) ELECTRIC FIELDS ON ANIMALS OF DIFFERENT AGES

Moscow GIGIYENA I SANITARIYA in Russian No 8, Aug 81 (manuscript received 24 Nov 80) pp 18-19

[Article by I. P. Kozyarin, Kiev Medical Institute imeni Academician A. A. Bogomolets]

[Text] In recent years, the attention of hygienists, biologists, pathophysiologists and other researchers has been drawn to a new problem, that of investigating the biological effects and ecological significance of commercial-frequency electric fields (CFEF), the sources of which are high-tension power lines (PL). For this reason, each year there is an increase in number of people of different sexes, age and in different physiological conditions who are exposed to CFEF under both industrial and living conditions. However, there is not enough information about the biological effects of CFEF on man and animals.

Our objective here was to examine the comparative sensitivity of young (growing) and old animals to 50-Hz electric fields.

Our biological model consisted of 40 male white rats 1.5-2 months of age, weighing 90-100 g, and 1.5-2 years old, weighing 400-500 g, which were divided into 4 groups of 10 animals. The 1st group (young) and 3d (old) group served as a control, while the rats in the 2d and 4th groups were exposed daily to CFEF of 15 kV/m for 30 min a day, for 2 months. For this purpose, the animals were placed in special dielectric cages with simulated electric field of 50 Hz generated by means of high-voltage tank [oil] transformers.

We assessed the animals' condition on the basis of dynamics of body weight, static work capacity, summation-threshold index (STI), latency period (LP) of unconditioned reflex, duration of hexenal-induced sleep, overall exchange of gases and blood cholinesterase activity. These parameters were determined before the experiment (background data) and every 2 weeks during exposure.

At the end of the experiment, we tested the functional state of the thyroid by the radioisotope tracer method. We tested post mortem the morphological composition of peripheral blood, supravital stain of internal organs and coefficients of their mass, brain tissue cholinesterase activity, liver glycogen content and ascorbic acid content of adrenals, balance and interorganic distribution of trace elements (copper, molybdenum, iron and manganese) in tissues by the quantitative spectrographic method (A. N. Zaydel' et al.).

We submitted the results to statistical processing with calculation of Student-Fisher criteria, considering differences to be reliable with P<0.05. We compared the parameters of experimental groups of animals to data for control rats of the same age. The Table lists information about the condition of the animals at the end of the experiment.

Parameters of functional state of animals toward the end of the experiment with exposure to CFEF (M±m)

Parameter	Animal group			
	1 (control)	2 (15 kV/m)	3 (control)	4 (15 kV/m)
Body weight, g	153,9±5,4	143,7±7,3	459,4±24,6	449,0±18,9
STI, V	10,3±0,4	13,7±0,5**	11,2±0,5	15,2±0,5**
Unconditioned refl.LP,ms	52,7±1,4	67,7±2,7**	61,2±1,6	77,6±2,5**
Blood cholinesterase activity, mM/mℓ/h	118,3±3,3	152,8±3,9**	117,7±2,5	151,8±4,0*
Brain tissue cholinester. activity, mM/g tissue/h	1176,1±64,4	838,3±93,4*	1007,6±73,7	793,8±28*
Liver glycogen, mg%	1837,9±110,2	2672,8±133,6**	2663,2±106,5	3263,5±163,1*
Ascorbic acid, mg%	394,5±24,0	410,8±23,6	352,9±26,8	400,5±27,1

* $P<0,05$.
** $P<0,01$.

The studies conducted before and during the experiment failed to demonstrate reliable differences between experimental and control groups of animals with respect to weight, static work capacity, duration of hexenal sleep and general exchange of gases. The most marked changes were found in the nervous system. The 2d and 4th groups of animals presented a statistically significant increase of STI and unconditioned reflex LP 4 weeks after the start of exposure (15 kV/m), which reached a maximum by the end of the experiment. Thus, the STI of young animals (2d group) increased by 35% in this period and in old animals (4th group) it increased by 33%; LP increased by 29 and 25%, respectively, as compared to the control. The demonstrated functional changes in the nervous system of experimental animals under the influence of CFEF were apparently related to impairment of dynamic equilibrium between excitatory and inhibitory processes in the cerebral cortex, with prevalence of the latter.

It was established in several works that changes are observed in blood cholinesterase activity, which is involved in the process of transmission of nervous impulses, under the influence of an electromagnetic field (EMF) (S. V. Nikogosyan; O. I. Shutenko, and others), which prompted us to include the study of this parameter in our studies. As can be seen in the table, exposure to CFEF elicited a decrease in brain tissue cholinesterase activity and increase in activity of this enzyme in the blood of the 2d and 4th groups of animals, a statistically significant increase in blood cholinesterase activity being observed in these animals after the 6th week of irradiation and up to the end of the experiment. This parameter increased by an average of 25% in the 2d group of rats and 23% in the 4th. In the opinion of some researchers (D. Ye. Al'pern and others), the increase in blood cholinesterase activity is one of the elements of adaptive and compensatory mechanisms with exposure to EMF. We cannot rule out the possibility that, in this case, the increase in blood

cholinesterase activity was caused by increased permeability of cell membranes in response to CFEF.

Two months after the start of the experiment, animals exposed to CFEF presented signs of stimulation of the thyroid, which were characterized by increased capacity of this organ to concentrate radioactive iodine; this is apparently related to the direct effect of the electric field on the functional state of thyroid cells.

During this same period, the 2d and 4th groups of animals (15 kV/m) showed a reliable increase in glycogen content of hepatic tissue (by 45 and 23%, respectively). Evidently, accumulation of glycogen in liver tissue was related to changes in functional state of the sympathoadrenal system.

The distinctions referable to balance and interorganic metabolism of trace elements (copper, molybdenum and iron) with exposure of animals to CFEF are of interest. Our study revealed that CFEF elicit a statistically reliable ($P<0.01$) increase in copper content of urine and feces of young animals (2d group) and decrease in excrements of old animals (4th group).

It is relevant to note that the changes in metabolism of manganese in two of its most important reservoirs presented different directions: the amount of manganese in bone tissue decreased and in hepatic tissue it increased. We also demonstrated an increase in manganese content of the liver, spleen, myocardium, teeth and skin of animals in the 2d and 4th groups, with considerable decrease thereof in skeletal muscles. There were changes in different directions with regard to blood manganese level: it dropped reliably ($P<0.05$) in young animals and rose in old ones ($P<0.05$), i.e., there was impairment of Mn homeostasis.

As for molybdenum, iron and manganese, we demonstrated an increase in levels thereof in excreta of both experimental groups of animals.

The changes in metabolism of the above trace elements in different organs and tissues of young animals, as compared to old ones, in response to CFEF are apparently related to their structural distinctions, circulation, intracellular metabolism, which are attributable to the animals' age and are adaptive in nature.

Examination of peripheral blood morphology failed to demonstrate changes in number of erythrocytes, leukocytes, reticulocytes and eosinophils in the 2d and 4th groups of animals. Analogous findings were made with regard to adrenal ascorbic acid content, supravital stain of internal organs and coefficients of their mass.

Conclusions

1. Brief exposure to CFEF in the course of a day within the range of intensities encountered in a real situation elicits changes in functional state of the nervous system and thyroid, some aspects of metabolic processes, trace element balance and interorganic metabolism in experimental animals.

2. Young animals are more sensitive to CFEF than old ones.

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METEOROLOGICAL RADAR AS SOURCE OF SHF ELECTROMAGNETIC FIELD ENERGY AND PROBLEMS OF ENVIRONMENTAL HYGIENE

Moscow GIGIYENA I SANITARIYA in Russian No 2, Feb 82 (manuscript received 11 May 81) pp 7-11

[Article by Yu. D. Dumanskiy, N. G. Nikitina, L. A. Tomashevskaya, F. R. Kholyavko, K. S. Zhupakhin and V. A. Yurmanov, Kiev Scientific Research Institute of General and Urban Hygiene imeni A. N. Marzeyev; Main Geophysical Observatory imeni A. I. Voyeykov; Central Aerological Observatory]

[Text] Meteorological radar stations (MRS) are intended primarily to monitor the condition of the environment. At the same time, when operating MRS, electromagnetic energy in the superhigh-frequency (SHF) range is emitted into the environment, and its level fluctuates over a wide range, depending on the distance to the radiation source (MRS). Hence, a meteorological radar device (MR), as a source of SHF energy with high biological activity, is a device that can have a certain effect on the environment and, first of all, the public.

For this reason, by assignment from the USSR State Committee for Hydrometeorology and Monitoring the Environment, the Kiev Scientific Research Institute of General and Urban Hygiene imeni A. N. Marzeyev, together with the Main Geophysical Observatory imeni A. I. Voyeykov and Central Aerological Observatory, conducted a study of the electromagnetic situation at locations of MRS and biological implications of electromagnetic fields generated by radar devices used for meteorological purposes.

First of all, it was necessary to determine the specifications of the MRS and their operating modes, establish the patterns of distribution of electromagnetic energy generated by MRS in the environment. A method was developed for this purpose, to measure electromagnetic fields in the SHF range using instruments and calculations.

On the basis of the obtained data, it was determined that all meteorological radar devices can be divided into three main groups. The first is referable to radar devices of the MR type, intended for determining the position and intensity of cloud cover, the second refers to the Meteorit (Meteor) and Meteorit-2 types of radar devices that are used as radiosondes to obtain

information about the free atmosphere and the third is referable to radar used to determine the position, nature and intensity of thunder clouds, detection of tendencies toward hail formation and guiding ground-based active anti-hail equipment (ARS-3M, Grad-2, Uragan, RMP-2) on the hail-forming clouds.

These radar devices operate in a pulsed mode of radiation in the wavelength ranges of 0.8, 3, 10 and 17 cm. Each type of MR usually operates at one particular wavelength. However, some of them have two working channels. For example, the MRL-1 can operate simultaneously over two channels, if necessary, emitting electromagnetic waves in the ranges of 0.8 and 3 cm.

Radar devices that are intended for locating the position and intensity of cloud formations operate in the mode of circular scanning, with the antenna turning over the azimuth at the rate of 6 r/min. The antennas have scanning limits, with regard to angle, ranging from -1 to 105°, and in addition, scanning can be done at angles of up to 10° with a 30-s period. The mode of the MR can be described as periodic. In cloudy weather, radar devices of this type operate 20-30 min every other hour and in clear weather, every 2-3 hours or less. Hence, this group of MR emit into the environment SHF electromagnetic field energy that is spatially and temporally intermittent, due to the circular movement of the antenna and scanning elevation [angular altitude], while the time intermittence is related to the mode of MR operation.

Radar devices intended to accompany radioisotopes when probing the atmosphere and the ones for protection against hail also operate in an intermittent mode. However, their intermittent operation differs appreciably from the operating modes of the first group of MR, with regard to both the time and spatial features. The results of statistical processing of time modes of MR operation in different seasons, in three climate zones, are listed in Table 1, which shows that MRS operating time constitutes 4.6 to 10.8 h/day. We should also call attention to the fact that MR referable to the third group and used for protection against hail operate only 4-5 months out of the year, and not every day.

Table 1. Mean parameters of time modes of MRS operation

Climate zone	Season	Times MR were turned on	Daily operation of MR, h
Subarctic	Winter Summer	9 14	4,6 6,2
Temperate	Winter Summer	18 23	8,4 10,8
Subtropical	Winter Summer	18 12	8,6 5,8

Table 2.
EFD ($\mu W/cm^2$) generated by MR

MR	EFD at distances of					
	100 м	200 м	300 м	500 м	1000 м	3000 м
MRL-1	4000	983	440	157	39	5
Meteor	45	11	5	1	—	—
ARC-3	9	6	4	4	1	—

After determining the technical and mode distinctions of MR operation, we studied the distribution of the SHF electromagnetic fields in three climate zones of the USSR where there are MRS. In each zone we studied at least 10 sources of SHF magnetic field radiation. This work was done using both instrumentation methods as developed by us ("Methodological Instructions," 1977) and calculation. In the instrument studies we used a PZ-9 measuring instrument to determine energy flux density (EFD) in both the free path and inside buildings. At first, we made theoretical estimates of EFD using technical data on the MRS studied, then used instruments to pinpoint the EFD level in free territory, with consideration of its profile. The results of these studies, which are listed in Table 2, revealed that the MR on free territory generate EFD of 1 to 4000 $\mu W/cm^2$. It should be noted that primarily the distance between the irradiation site and radiation source, as well as vertical angle of antenna radiation, have an appreciable effect on EFD. With negative angles of antenna radiation, EFD increases drastically in the area where the public is exposed. The level of installation of the MR above the ground also exerts a significant influence. The higher it is, the lower the EFD level in the zone where there are people.

Thus, the results of these studies revealed that MR are rather powerful sources of SHF electromagnetic fields, the effects of which on the public are related to space and time. MRS, as a source of emission of electromagnetic energy in the SHF range, merit tenacious scrutiny, both from the standpoint of elaborating hygienic requirements for placement thereof and regulation of SHF energy in inhabited areas. One should pay attention to the fact that the existing health standards and rules for location of sources of SHF radiation do not entirely reflect the operating and technical distinctions of MRS, so that even now there is a need to revise them. For this purpose, it is necessary, first of all, to do the following: determine the maximum actual SHF burden on man in residential [populated] areas; conduct biomedical studies to determine the dose-time functions of effects of SHF fields with different wavelengths; elaborate hygienic standards for SHF fields for residential areas, with due consideration of actual modes of MRS operation, in a differentiated manner with respect to wavelength and actual exposure time; formulate hygienic requirements for placement of MRS. Investigation of the biological activity of pulsed electromagnetic fields in the 3-cm range of waves was one of the phases of a combined study. Field and exposure levels were selected on the basis of those demonstrated in residential areas.

These studies were conducted on 1200 mongrel albino rats of the same sex, which were used in a 6-month chronic experiment (4 months of exposure and 2 months thereafter). The animals were exposed for 12 h/day in anechoic chambers made of a special radio-absorbing material. This permitted uniform distribution of the electromagnetic field both throughout the chamber and irradiation sites.

Table 3.
Some physiological parameters of albino rats exposed continuously to 3-cm waves in pulsed mode (M±m)

EFD, μW/cm²	Static endurance (min) with exposure time of		Electrodermal sensitivity (min with exposure time of	
	90 days	120 days	90 days	120 days
40	7,7±0,43	7,5±0,54	41,8	42
P	<0,05	<0,05	<0,05	<0,05
25	8,0±0,43	7,7±0,43	38,2	39
P	<0,01	<0,05	<0,01	<0,05
10	9,0±0,75	8,9±0,64	38,1	37,6
P	>0,01	>0,01	>0,01	>0,01
Control	8,9±0,97	8,9±0,97	37,9	37,8

The animals were divided into groups according to EFD (115, 60, 40, 25, 10 and 5 μW/cm²). As a control, we used intact animals kept under equivalent conditions. Their functional state was evaluated on the basis of physiological, biochemical and immunological parameters.

The physiological parameters included a set of behavioral reactions which are highly sensitive to physical factors and permit an integral evaluation of condition (threshold of sensitivity to electrodermal stimulation, static work capacity and conditioned reflex activity using alimentary-motor method).

The results of these studies revealed that the threshold increased by 1.5-1.1 times and static work capacity decreased to one-half with EFD of 115 and 60 μW/cm² (Table 3) by the end of the exposure period. Conditioned reflex activity of animals exposed to electromagnetic fields with EFD of 40 and 25 μW/cm² or more was characterized by a change in latency period of conditioned reflexes ($t = 3.27$ and 3.01), 1.4 and 1.1-fold decline of motor reaction to a positive conditioned stimulus and elimination of positive conditioned reflex in response to a bell. Thus, analysis of the results of the physiological studies revealed a change in functional state of the muscular and receptor systems, as well as central nervous system, under the influence of SHF fields with EFD of 115-25 μW/cm², which is indicative of prevalence of inhibitory processes (Yu. D. Dumanskiy et al.; A. M. Serdyuk; Yu. A. Kholodov; M. I. Yakovleva).

Concurrently with the above-described studies, a study was made of biochemical parameters of animals in other groups of a similar chronic experiment, which characterized enzymatic processes (activity of blood cholinesterase and metalloenzymes of blood serum), protein metabolism (urea and residual nitrogen in blood), carbohydrate metabolism (glycogen content of hepatic tissue), as well as parameters of functional state of the neurohumoral system (catecholamine content of adrenals and brain tissue, blood plasma ACTH activity, ascorbic acid content of adrenals).

The results of these studies, which are listed in Table 4, indicate that there was change in cholinesterase activity as a function of level of exposure. With EFD of 115 μW/cm², there was inhibition of this enzyme for the first 2 months and with EFD of 40 μW/cm² there was activation after the 1st month. In both cases, this parameter reverted to normal by the end of the exposure period. Lower intensities of SHF fields did not elicit deviations in cholinesterase content, as compared to the control.

Table 4. Some biochemical parameters of albino rats under the continuous effect of pulsed electromagnetic field in third range (M±m, n = 10)

Parameter	EFD, μW/cm²	Exposure time, days		
		30	60	120
Blood cholinesterase activity, fig/min/100 ml.	115	98,71±9,64	103,5±5,96	116,86±4,99
	40	159,6±4,33	128,8±6,06	130,8±7,03
	Control	123,0±4,22	131,0±7,03	126,9±3,35
Ceruloplasmin activity relative units	115	0,70±0,03*	0,67±0,04*	0,66±0,44
	40	0,59±0,14	0,56±0,016	0,60±0,017
	Control	0,55±0,18	0,56±0,017	0,57±0,017
Liver glycogen, mg%	115	852±93,2*	950±64,3	1001±52,9*
	40	1522,0±79,0	1486±71,43	1163±75,75
	Control	1417±81,17	1572±91,9	1305,0±54,1
Brain tissue epinephrine	40	—	0,153±0,009	0,158±0,006*
	25	—	0,15±0,007	0,155±0,006*
	10	—	0,13±0,007	0,14±0,009
	Control	—	0,14±0,01	0,13±0,009
Brain tissue norepinephrine	40	—	0,203±0,013	0,18±0,015
	25	—	0,21±0,01	0,20±0,015
	Control	—	0,20±0,013	0,21±0,012
Blood plasma ACTH	40	—	25,1±1,77	23,0±2,07
	25	—	26,7±1,8	24,8±2,7
	Control	—	26,57±2,12	25,7±1,81

*Figures are statistically reliable.

In addition, we observed an increase in ceruloplasmin activity (by 15-20%) and iron content of transferrin (P<0.01) in blood serum under the influence of SHF fields with intensities of 115 and 60 μW/cm² throughout the exposure period.

The demonstrated changes in enzyme systems could be largely attributable to the status of ultrastructure of the biological membranes under the influence of SHF fields, which could have led to impairment of various metabolic processes (Yu. D. Dumanskiy and L. A. Tomashevskaya; V. G. Lazarovich; A. M. Serdyuk).

Changes in end products of protein metabolism, such as urea and residual nitrogen, were observed with SHF fields of 115 and 60 μW/cm². These changes consisted of a statistically reliable increase to 25-27% in urea content, as well as 15% increase in residual nitrogen of blood serum with exposure to EFD of 115 μW/cm².

The above disturbances in protein metabolism were associated with changes in carbohydrate metabolism. Hepatic glycogen content dropped by 20-25% (P<0.01) in experimental animals under the influence of electromagnetic energy with EFD of 115 μW/cm². Such changes in protein and carbohydrate metabolism were indicative of possible prevalence of dissimilation processes under the effect of this factor. In addition, we determined catecholamine levels in organs (brain and adrenals), blood plasma ACTH activity and ascorbic acid content of the adrenals in relation to their mass in animals exposed to EFD of 40, 25 and 10 μW/cm². As a result, we demonstrated a 10% elevation of brain tissue epinephrine level by the end of the period of exposure to this factor with

intensities of 40 and 25 $\mu W/cm^2$, with 21.5 and 10% rise in the adrenals. The other parameters remained unchanged. This indicated that the neurohumoral system is involved in the reaction to electromagnetic energy, possibly by involving certain humoral elements.

Thus, the results of biochemical studies revealed that chronic exposure to a pulsed electromagnetic field in the 3-cm range of waves, with continuous generation at EFD of 115-25 $\mu W/cm^2$, affects metabolic processes in experimental animals. The changes observed were mainly in the same direction and did not reach a pathological level.

Thus, this set of biological and hygienic studies revealed that the electromagnetic field emitted by MR is a biologically active environmental factor, which should be submitted to hygienic regulation with setting of differentiated hygienic standards for the public.

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EFFECTS OF MICROWAVE RADIATION ON MOUSE HEMOPOIETIC STEM CELLS AND ON ANIMAL RESISTANCE TO IONIZING RADIATION

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 4, Jul-Aug 81 (manuscript received 11 Aug 80) pp 558-562

[Article by D. Rotkovska, A. Vacek and A. Bartonickova, Institute of Biophysics, Czechoslovak Academy of Sciences, Brno]

[Text] The effects of microwaves (MW) on hemopoiesis in mice are discussed. Stimulation of colony-forming capacity of bone marrow and the spleen was demonstrated after total-body exposure of mice for 5 min at the parameters used. This MW effect was used to enhance mouse resistance to ionizing radiation.

The question of biological effects of electromagnetic waves in the radiofrequency range has still been little-studied. From the standpoint of interaction with biological objects, electromagnetic waves of less than 1 m (so-called microwaves--MW) are of the greatest interest. Maximum absorption of electromagnetic energy is observed in this range, and there is intensive interaction with living matter; the final effect depends on both the physical parameters of MW and properties of the irradiated biological object. According to data in the literature [1-5], MW are a rather active physical factor. Electromagnetic fields in the centimeter range, with radiation intensity of the order of hundreds of mW/cm^2, could lead to damage of an organism and death [1].

Most of the previously published works have dealt with examination of the physical condition of individuals who are exposed to this physical factor [2-4]. Some authors were concerned with changes in blood. A decrease in erythrocytes and hemoglobin of rat peripheral blood was demonstrated in the case of chronic irradiation [5]. Rats presented early (1st-3d day) increase in leukocytes, lymphocytes and neutrophils after 7-h exposure to MW with intensity of 20 mW/cm^2, with normalization by the 7th postradiation day [6]. Changes in peripheral blood, which depended on wavelength, time and intensity of exposure, were demonstrated by other authors too. Increased uptake of radioactive iron in erythrocytes, which was at a maximum 45 days after exposure, was observed in dogs exposed to MW at an intensity of 100 mW/cm^2 for 7 h [7]. Chronic exposure to MW at low intensities resulted in an increase in erythrocyte count, changes in structure of nuclei and in erythroblast

cells of bone marrow, as well as lymphocytes in lymph nodes and spleen of rats and guinea pigs [8]. MW were also used in combination with ionizing radiation [9-11]. Exposure of Chinese hamsters to MW (2.45 GHz, 60 mW/cm^2) 5 min after ionizing radiation raised $LD_{50/30}$ from 8.21 to 8.54 Gy.

According to the literature, the effects of MW on hemopoiesis were assessed primarily on the level of peripheral blood. Some of the findings are rather contradictory, most probably due to differences in set-up of experiments and radiation sources used. In spite of this, some tendency toward stimulating hemopoiesis was observed. We decided to test in this study the possibility of such stimulation in experiments on mice, and to use MW as a factor to modify mouse resistance to ionizing radiation.

Material and Methods

Experiments were conducted on female C57/Bl/10 mice 8-10 weeks of age. The Microdiaterm Prema (CSSR) unit, which was specially modified for exposure of small laboratory animals, was used to deliver MW. They were exposed under the following conditions: frequency 2.45 GHz, intensity 100±10 mW/cm^2, in a special plexiglas chamber permeable to electromagnetic waves, with constant exchange of air. The animals were submitted to total-body exposure for 5 min. In order to evaluate the thermal effects of MW, we measured rectal temperature (with a thermocouple) before and after exposure to MW, and made dynamic studies of temperature changes over the entire body surface of the mice by means of an Aga 680 infrared thermovision camera [12]. Ionizing radiation was delivered from a TUR x-ray unit at 200 kV, 20 mA, with 0.5 mm Cu + 0.5 mm Al filters, focal distance 50 cm and dose rate of 2.61×10^{-4} A/kg. We used the following hematological methods: method of exogenous spleen colonies [13], method of incorporation of radioactive iron in erythropoietic organs; counting cellularity of the spleen and femoral bone marrow; a Coulter Counter, model Fn, was used to assay peripheral blood leukocytes. The data were submitted to statistical processing using the Student test and χ^2 test.

Results and Discussion

Thermal changes: We found that rectal temperature rose by a mean of 2.3±0.2°C in the course of 5-min exposure to MW. Dynamic measurement of temperature with the thermovision camera during 5-min exposure to MW showed that organs with the highest blood content (heart, spleen, liver) underwent the most intensive heating. Evidently, such nonuniform elevation of temperature is attributable to nonuniform absorption of electromagnetic energy in tissues, along with manifestations of physiological changes as the body's reaction to elevation of temperature. However, within 5 min after exposure to MW there was a return to the initial distribution of body temperatures (for more details, see [12]).

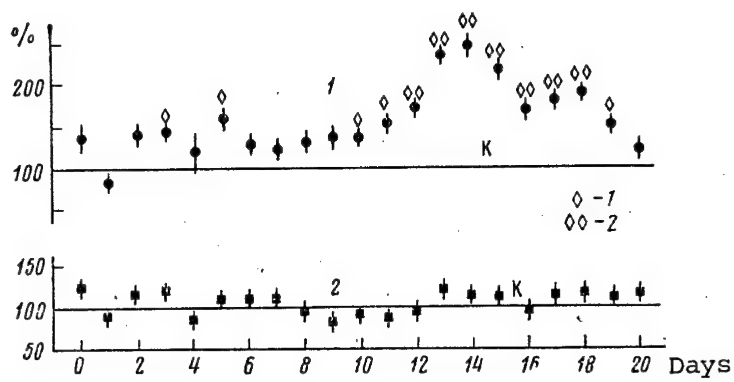
Effect of MW on hemopoiesis: Before performing transplants, donor mice were exposed to MW. The mice were sacrificed at different postexposure times; suspensions were prepared of the spleen and bone marrow and injected intravenously in amounts of 10^6 cells for the spleen and 10^5 for bone marrow to recipients exposed to x-rays in a dosage of 154.8 mC/kg. The results revealed that MW can activate hemopoietic stem cell populations and enhance

their repopulation capacity (Table 1). The effects of MW were also manifested in the differentiating compartment; incorporation of radioactive iron in hemopoietic organs showed fluctuating increase in erythroid differentiation in the spleen of mice exposed to MW, starting on the 2d-3d day after exposure and reaching a maximum at the start of the 3d week (Figure). At the same time, there was an increase in quantity of leukocytes and erythroid cellularity in the spleen after exposure to MW, which is probably indicative of increased blood supply to this organ (Table 2, 2 h after exposure).

Table 1. Changes in colony-forming capacity of the spleen and femoral marrow at different times after exposure to MW [CFU--colony-forming units]

Time after MW	Number of recipients	CFU in	
		spleen	femur
Control	10	349±79	654±82
2 h	10	689±86*	810±90
6 h	10	609±40*	1061±112*
12 h	10	485±47	666±48
24 h	11	644±43*	711±54
7 days	10	612±48*	854±84
14 days	10	761±68**	1187±110**

* $P < 0{,}05$; ** $P < 0{,}01$.



6-Hour incorporation of ^{59}Fe in spleen (1) and bone marrow (2) at different times after exposure to MW. X-axis, days after MW: y-axis, level of tracer incorporation, % of nonexposed control (K)

1) P<0.05 2) P<0.01

We then tested the effect of elevated ambient temperature, which elicited the same change in rectal temperature as MW (Table 3). The results of these experiments revealed that raising ambient temperature only partially resembles the effects of MW on colony-forming capacity of bone marrow and spleen, and

then only in the interval of 2 h after exposure to heat (for the sake of brevity, other intervals are not listed in Table 3). This is most probably related to the stressor effect of heat.

Table 2. Leukocyte content of peripheral blood, cellularity of spleen and bone marrow at different times after MW

Time after MW	Number of mice	Leukocytes $\times 10^3/mm^3$	Cellularity: spleen, erythrocytes $\times 10^8$	Cellularity: spleen, karyocytes $\times 10^8$	Cellularity: bone marrow, erythrocytes $\times 10^7$	Cellularity: bone marrow, karyocytes $\times 10^7$
Control	5	10,60±0,51	4,00±0,27	1,23±0,07	3,32±0,03	1,24±0,05
2 h	5	10,03±0,72	5,40±0,12**	1,80±0,20*	4,52±0,14**	1,57±0,08*
24 h	5	16,00±1,53*	4,92±0,45	1,55±0,20	3,34±0,21	1,32±0,05
3 days	5	16,30±0,58*	5,01±0,37	1,32±0,05	3,28±0,13	1,32±0,06
5 "	5	16,40±1,53*	5,03±0,38	1,22±0,27	3,94±0,21*	1,38±0,07
7 "	5	10,43±0,97	5,03±0,36	1,67±0,26	2,98±0,13	1,41±0,08
14 "	5	13,20±1,26	5,61±0,42*	1,83±0,13*	3,12±0,17	1,21±0,06

* $P < 0,5$; ** $P < 0,01$.

Table 3. Changes in colony-forming capacity of the spleen and bone marrow at different times after exposing mice to elevated ambient temperature (T)

Time after T	Number of recipients	Number of CFU in spleen	Number of CFU in femur
Control	10	349±79	654±82
2 h	10	435±60	734±20
6 h	9	239±38	359±29*
12 h	10	194±36	416±90
24 h	10	251±28	551±62

* $P < 0,01$.

It can be concluded that exposure to MW activates stem cell populations. This effect is also manifested in the differentiated cellular compartment at the relatively late stage after exposure to this physical factor. Perhaps, elevation of ambient temperature, improved delivery of blood to organs and, consequently, improved delivery of oxygen to tissues with exposure to MW lead to some enzymatic and metabolic activation of resting cells and enhancement of their proliferative and differentiating capacities [14].

Effect of MW on animal resistance to ionizing radiation: It was shown that MW used before exposure to lethal x-radiation increases animal survival rate (Table 4). The increased resistance of mice to x-radiation immediately after exposure to MW is most probably stimulated by a nonspecific stressor effect. The increased resistance of animals exposed to x-radiation

14 days after MW is probably attributable to an increase in CFU pool elicited by MW. This is manifested by both the parameters of peripheral blood and on the level of hemopoietic stem cells of bone marrow and spleen (Tables 1 and 2). In control experiments, where the effect of elevated ambient temperature on animal resistance to ionizing radiation was tested, no changes were demonstrable (Table 4; for the sake of brevity, only the 5-min interval is listed).

Table 4. 30-Day survival after exposure to x-radiation (XR) and MW as a function of interval between these factors

Groups and intervals between factors	Number of animals	Deaths	Survivals	Survival rate, %
XR, control	23	9	14	61
T + XR, 5 min	20	9	11	55
MW + XR, 5 min	20	2	18	90*
MW + XR, 24 h	21	12	9	43
MW + XR, 72 h	22	15	7	32*
MW + XR, 14 days	24	2	22	92*

* $P < 0{,}05$.

According to the results of these studies, MW can activate both the stem and cellular differentiating compartment of hemopoietic organs. Since it is not feasible at the present time to adequately heat internal organs by other methods, we still do not know whether the effects of MW are attributable to thermal or specific factors. We were unable to find any studies in the available literature concerned with such a problem on the level of hemopoietic stem cells. The results of the experiments where both types of radiation were combined indicate that it is feasible to use the stimulating effects of MW on hemopoiesis.

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EFFECT OF SINGLE EXPOSURE TO MICROWAVES ON QUANTITY AND FUNCTIONAL PROPERTIES OF T AND B LYMPHOCYTES OF GUINEA PIG AND MOUSE SPLEEN

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 4, Jul-Aug 81 (manuscript received 28 Jan 80) pp 626-629

[Article by I. A. Rudakov, S. F. Rudakova, I. V. Rozhinskaya and O. S. Ogurtsova, Scientific Research Institute of Medical Radiology, USSR Academy of Medical Sciences, Obninsk]

[Text] Change in immunological reactivity of the exposed organism is one of the important elements of the biological effects of microwaves. Animals chronically exposed to SHF fields of nonthermal intensity present intensification of lymphocytopoiesis [1, 2], stimulation of spontaneous and mitogen-induced blast transformation of lymphocytes [3]; immunization of chronically irradiated animals is associated with more marked increase in antibody-forming cells (AFC) in lymph nodes than in the control [4]. Conversely, microwaves of thermal intensities elicit depression of immunological reactivity in a number of instances [5, 6]. However, there are still very few data on the immunological status of irradiated organisms as a function of exposure to SHF fields of different ranges and there is virtually no information about the severity and duration of immunological changes in the case of single exposure to high-intensity microwaves. For this reason, our objective was to study several parameters of cellular immunity of animals at different intervals following single exposure to microwaves of thermal intensity.

Material and Methods

The first series of experiments was performed with guinea pigs weighing 300-400 g, who were submitted to single total-body exposure to microwaves in the reactive zone using a Luch-58 unit (frequency 2375 MHz, distance from emitting antenna horn 30 cm, output power 100 W, exposure 15 min). As a result of such exposure, the animals' body temperature rose by 4-4.5°C. Immediately after irradiation, as well as 1, 4, 7 and 21 days later, the animals were sacrificed; the spleen was excised under sterile conditions and a pooled suspension of spleen cells from 3-5 animals was obtained, which was then used to assess spontaneous and concanavalin A-induced (end concentration in cultures 0.5 to 10.0 μg/mℓ) lymphocyte blast transformation by recording radioactivity of ^{3}H-thymidine incorporated in DNA. We examined at least three cultures at each experimental point. In the second series of experiments, adult male

CBA mice weighing 20-22 g were submitted to single total-body irradiation from a Luch-58 unit at 40 mW/cm^2 for 30 min, with 60 cm distance from the emitting antenna horn. We assessed the lymphocyte blast transformation reaction of pooled mouse spleens immediately after irradiation, 3 h, 1, 3 and 7 days later. In addition, we counted the total nuclear cells in the spleen, percentage of T cells (determined in the cytotoxic test using rabbit serum against mouse thymus, depleted with erythrocytes, hepatic and bone marrow cells of mice [7]) and B cells with complement receptors on their surface (determined by the method of rosette formation with sheep erythrocytes loaded with antibodies and mouse complement [7]). In the third series of experiments, at different post-exposure intervals (under the same conditions as in the second series), we immunized mice by intraperitoneal injection of sheep erythrocytes (5×10^8 per mouse), and assayed nuclear cells, T and B lymphocytes in the spleen 4 days later (using methods described for the second series of experiments), as well as AFC according to Cunningham--gel-free local hemolysis, which demonstrates mainly cells that form 19 S antibodies (IgM) with the highest hemolytic activity [8]. Intact immunized mice, as well as nonimmunized animals, served as a control.

Results and Discussion

Table 1 lists data on degree of blast transformation of lymphocytes in the pool of guinea pig spleens at different times after exposure to microwaves. The index of stimulation of intact guinea pig lymphocytes constituted 39.7 with an end concentration of mitogen of 10 μg/mℓ; immediately after exposure, this index dropped somewhat, but subsequently, throughout the observation period, the stimulation index of irradiated animals was almost half the value of intact guinea pigs. Similar changes were observed with other concentrations of mitogen; no stimulation of lymphocytes was demonstrable in irradiated guinea pigs with a concentration of 0.5 μg/mℓ. Analogous changes in the direction of decline of functional activity of T lymphocytes of the spleen, as evaluated by the blast transformation reaction, were noted in irradiated mice (Table 1).

Table 1. Mean values of index of lymphocyte stimulation for guinea pig and mouse spleen as a function of postradiation time and concentration of concanavalin A

Animal species and postradiation time	Concanavalin A concentration, μg/mℓ				
	0,5	1,25	2,5	5,0	10,0
GUINEA PIGS					
Nonirradiated control	2,1	13,1	23,0	30,7	39,7
30 min	—	3,7	15,1	24,8	26,8
1 day	—	3,4	10,5	13,3	21,2
4 days	—	4,2	7,9	14,2	20,6
7 "	—	4,3	10,9	12,8	22,6
21 "	—	4,1	9,3	11,1	21,0
CBA MICE					
Nonirradiated control	2,3	7,1	23,8	89,8	—
30 min	1,3	10,1	23,1	36,0	—
3 h	0,5	1,9	9,9	18,6	—
1 day	1,2	3,3	12,0	—	—
3 days	—	1,2	13,4	20,3	—
7 "	1,0	5,2	12,2	28,6	—

Note: The stimulation index was determined as ratio of number of pulses/min in cultures with and without the mitogen

Table 2. Number of nuclear T and B lymphocyte cells and AFC in mouse spleen after immunization at different times following irradiation from Luch-58 unit

Factor	Number of mice	Days after exposure	Nuclear cells, $\times 10^6$	T cells		B cells		AFC	
				%	$\times 10^6$	%	$\times 10^6$	per 10^6 spleen cells	for entire spleen $\times 10^3$
Immunized control	9		87,0±7,9	36,0±1,3	31,6±2,9	22,8±2,1	20,8±3,3	440±47	38,8±5,8
Irradiated control	5	4	48,4±3,4*	57,5±3,9*	27,3±2,2	9,8±0,8*	4,9±0,7	0	0
	5	12	47,7±5,6*	44,6±1,1*	21,1±2,5	19,4±1,0	9,2±1,0	—	—
Irradiation + immunization	5		61,5±2,8*	45,4±0,6*	27,9±1,3	24,4±1,9	15,1±1,7	490±58	29,5±3,4
	5	3	56,4±5,28*	—	—	13,6±0,7*	7,7±0,9	811±157*	48,8±13,2
	4	7	84,5±8,4	35,3±1,1	30,2±3,4	5,0±0*	4,2±0,4	923±142*	72,5±7,4
	5	13	76,6±3,7	32,2±1,1	24,5±1,2	17,8±1,6	13,3±1,0	456±112	34,7±9,0
	5	28	165,4±6,4*	35,8±1,2	59,3±3,2	26,6±2,4	44,8±5,3	552±98	94,6±18,9
	4	34	85,2±21,9	43,5±0,4*	37,0±9,5	18,0±1,4	14,4±3,7	640±61*	56,2±16,7

*Data that differ reliably from the results of corresponding control group (P<0.05)

Study of the quantitative correlations between lymphocyte populations of the mouse spleen at different postradiation intervals revealed a tendency toward increase in T cells (to 32-51%, versus 30% in the control) for the first 3 postradiation days, as well as fluctuating changes in number of nuclear cells. There was no appreciable change in number of B lymphocytes.

As can be seen from the results listed in Table 2, after immunizing irradiated animals the number of spleen karyocytes increases as a function of time between irradiation and immunization. Moreover, irradiation alone elicited an increase in percentage of T cells, as compared to the intact, nonimmunized control. All of the parameters studied, with the exception of cellularity of the spleen, of animals immunized immediately after irradiation corresponded to the immunized control. However, 3 and 7 days after irradiation, in the presence of decreased percentage of B lymphocytes, there was an increase (by 1.5-2 times) in AFC. After 28 days, there was an increase in overall cellularity of the spleen; the percentage of T and B cells corresponded to the immunized control and there was some increase in AFC. A reliable increase in AFC was also demonstrated in animals immunized 34 days after irradiation.

Thus, we observed an increase in effectiveness of the response of the lymphoid population to antigenic stimulation in animals immunized at the early stages following exposure to microwaves of thermal intensity. This is apparently related to intensification of B cell function caused by the SHF field, and they actively change into antibody-secreting plasma cells. The increase in functional activity of B cells is perhaps aided by intensified spontaneous proliferation of T lymphocytes caused by microwave radiation.

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MAIN DIRECTIONS OF SOVIET RESEARCH ON BIOLOGICAL EFFECTS OF MICROWAVE RADIATION

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[Article by M. G. Shandala, M. I. Rudnev, Ye. F. Stoyan and G. I. Vinogradov (Kiev)]

[Text] Microwave radiation as a physical environmental factor is an independent hygienic problem, the importance of which in the man-environment system is constantly growing, since this factor has already gone beyond the limits of industrial deleterious factors and has changed into a factor of inhabited areas.

There are a considerable number of experimental and survey works in the Soviet and foreign literature dealing with the effects of microwaves on living organisms (M. G. Shandala; Yu. D. Dumanskiy et al.; A. M. Serdyuk; B. M. Savin and N. B. Rubtsova, and others). The submitted data are not always homogeneous, in some cases they are contradictory and insufficiently validated, which makes it necessary to activate scientific work on the problem of biological activity of microwave radiation.

The focal aspect of this problem is referable to scientific substantiation of hygienic standards, i.e., setting thresholds of the adverse (deleterious) effect of this factor, so that for the last few years Soviet researchers concentrated mainly on investigation of the effects of low-intensity microwaves, ranging from 1 to 1000 $\mu W/cm^2$.

We consider biological validation of standards on the basis of experimental research and studies of the health status of individuals residing in areas where this factor is present to some degree to be the only correct approach to the problem of setting standards for microwave radiation, like other environmental factors.

Strict simulation of irradiation conditions in animal experiments enables us to determine the nature, degree and main patterns of biological effects, including deleterious effect of the factor, as a function of its intensity, duration of exposure, wavelength and other variables. Special attention should be given to the choice of tests characterizing the functional state of the organism,

since in the area of environmental hygiene the criteria for setting standards for environmental factors should be the functional, rather than pathological, changes with due consideration of their significance to the whole organism. The latter is extremely complex, so that to be totally confident of the safety of standard levels, subthreshold levels are used in our country as the maximum permissible ones for the public, which do not elicit demonstrable functional changes in animals and man (M. G. Shandala; I. V. Sanotskiy et al.).

At the same time, it is natural for the organism to perceive and react to stimuli within a certain range, so that the demonstrated reactions per se are not necessarily indicative of the adverse nature of such factors, and it is necessary to assess their significance to the organism. Under some conditions and at a certain intensity, exogenous factors have informatively important significance to the organism and the adequate reactions to them are useful, under other circumstances they may play a negative part.

To answer these questions, it is necessary to accumulate as much information as possible, on the basis of experiments with animals and observation of people, about the significance not only of the magnitude, but biological importance of demonstrated reactions to the organism. The data should be submitted for the entire spectrum of intensity of a factor, ranging from total absence to high levels that are incompatible with life.

Apparently, different degrees of intensity of a factor elicit different reactions. As we see it, the zone of optimum intensity of a factor should be the range, in which the body's reactions are of an evolutionary adaptive nature. Demonstration of compensatory reactions is indicative of deviation of the factor in question from the optimum which, however, is not detrimental to the organism. It is only the appearance of regenerative reactions (reparative regeneration) that is indicative of the deleterious nature of the factor's effects and, consequently, inadmissible intensity thereof.

In view of the foregoing, when studying the biological effects of radiation of low intensity, one should primarily use the methods for studying defense and adaptive reactions of an organism and, with exposure to high intensities, the reactions that reflect deeper changes in functional state of the organism. Aside from intensity of a factor, hygienic standard setting must take into consideration duration of exposure to it, and this raises the problem of the dose approach to standard setting.

The typical distinction of research conducted in our country is the preference given to parameters of biological effects of microwaves in the case of long-term (up to several months) daily (from a few hours to around the clock) exposure of different species of animals (Yu. D. Dumanskiy et al.; M. O. Navakatikyan, and others). Much importance is also attributed to evaluation of quality of function of different body systems after discontinuing exposure to the factor (for 1 to 3 months) and with the use of functional tests on the organism or individual systems thereof, as well as reproduction of some form of pathology or other in animals (M. G. Shandala et al.).

Use of the system of step-by-step adaptation, which involves evaluation of body reactions in the presence of gradually increasing intensity of the factor

and use of functional tests, made it possible to determine that adaptive and compensatory-adaptive reactions develop with increase in intensity of a high-frequency field. With this experimental set-up, several patterns were demonstrated in the reactions of various body systems to microwaves, and it was concluded that doses of 500 and 50 $\mu W/cm^2$ elicit certain changes in the central nervous system, immunological and certain other body systems, whereas a dose of 10 $\mu W/cm^2$ stimulates compensatory-adaptive reactions and can be assessed as subthreshold, 1 and 5 $\mu W/cm^2$ levels being considered inactive.

Exposure to low-intensity factors may lead to integral functional disturbances in complex functional systems, let alone an animal, without overt changes in different elements of the system. Integral parameters reflect nonspecific changes in an organism; with exposure to low intensities of a factor they do not necessarily indicate that the changes are undesirable, and for this reason they require physiological and hygienic interpretation.

One of the most important integral parameters in evaluating the effects of environmental factors is the functional state of the central nervous system and behavior of animals.

It has been established under experimental conditions that exposure to low levels of microwave radiation leads to impairment of bioelectric processes in different parts of the brain, followed by change in excitability and lability of neurons. Periodic change in frequency potentials was directly related to prevalence of excitatory or inhibitory processes in the cortex (Yu. A. Kholodov; A. M. Serdyuk, and others).

It is difficult to analyze data in the literature concerning the effects of microwaves on animal behavior because of the diversity of study methods and irradiation modes used; however, most authors report a change in behavioral reactions with long-term exposure to levels that are close or equal to the maximum permissible levels (Ch. Ch. Asabayev et al.; Yu. D. Dumanskiy et al.; M. O. Navakatikyan; Yu. A. Kholodov et al., and others). Formation of conditioned reflexes is impaired, and there is a change in activity of unconditioned food reflexes. In some cases, there are phasic functional changes: the effects vary in direction, depending on the level or duration of exposure, and it was found that exposure to wavelengths of 12.6 cm, as well as shorter waves were effective (N. P. Zalyubovskaya).

Analysis of the results of studying the effects of low-intensity microwaves on the central nervous system warrants the belief that functional changes therein are the result of interaction of different systems in the integral organism. The question of principal mechanisms of this effect has yet to be answered.

The state of the immune system is another important integral indicator of the effects of microwaves. Studies in this direction have concentrated on evaluation of cellular and humoral immunity, as well as nonspecific defense factors (G. I. Vinogradov; N. M. Gonchar). In recent years, works have been published that deal with the mechanisms of action of electromagnetic energy on the immune system. Investigation of the nature and severity of allergic processes, which

occur during exposure to an electromagnetic field, is important to evaluation of immunological reactivity of the organism to low-intensity microwave radiation (G. I. Vinogradov et al.).

Soviet specialists devote much attention in the studies of biological effects of microwaves to the functional state and other important systems--cardiovascular, respiratory, hemopoietic, endocrine, etc. (V. N. Nikitina; Ye. V. Gembitskiy; Ye. I. Obukhan; M. I. Rudnev et al.).

With increase in intensity of the natural electromagnetic background of earth, the problem of assessing the mutagenic hazard of low-intensity levels of microwave radiation acquires particular importance. It has been established on various test objects that such levels are capable of eliciting a mutagenic effect, the severity of which depends on exposure conditions, and can increase animal embryo death rate (G. I. Leonskaya et al.).

One of the most important directions of work on biological effects of microwaves is investigation of their effects on man. The existing clinical data pertain chiefly to people whose work involves exposure to microwaves (A. M. Serdyuk; K. V. Nikonova and A. Ye. Vermel', and others). A number of functional changes referable to different systems (nervous, cardiovascular, hemopoietic and others) have been found in personnel subject to nonthermal levels of this factor for a more or less extended time, and this leads to development of an entire group of symptoms, similar to the one that may be present under some other conditions: emotional and muscular strain, various chronic diseases, etc. It is indicated in several reports that neurological symptoms are prominent in the group of disturbances present in individuals who are regularly exposed to low-intensity microwaves (Yu. D. Dumanskiy et al., and others). It is stressed that the functional changes demonstrable in man are quite diverse; they do not always present clearcut signs and, in most cases, are reversible; however, when man is exposed for a long time to this factor the changes become quite persistent.

According to most researchers, the incidence and severity of objective and subjective symptoms depend on the intensity and duration of exposure to the factor, wavelength, nature of field (pulsed, static) and, mainly, work tenure involving exposure, i.e., overall duration thereof.

Simulation in experimental laboratories of real irradiation conditions, which exist in the industrial environment or populated areas, consistent with the nature of theoretical research, is another direction of investigation of the effects of low levels of electromagnetic energy on human health. Here, as is the case under industrial or clinical conditions, the main methodological approach is complex [combined] investigation of functional capacities of the organism during exposure to this factor, on the basis of evaluating various systems of man.

When conducting studies on volunteer subjects, one must rule out any influence that could elicit undesirable changes, so that in such cases subthreshold or close to such levels of intensity and exposure are used (Yu. D. Dumanskiy et al.; T. V. Kalyada et al.). Under such conditions, it is possible to detect early, preclinical forms of disturbances and adaptive changes due to exposure to microwaves.

Investigation of the functional state of man exposed to this factor for therapeutic purposes is one of the possible means of obtaining information about the biological effects of microwaves. There is no information concerning the results of a comprehensive, systematic study of this population group.

In recent times, efforts have been made to study the effects of electromagnetic waves in the radiofrequency range on the public living in an area where such waves exist (L. A. Tomashevskaya and V. M. Popovich; A. M. Serdyuk, and others). The study of biological effects of low levels of this factor in the field involves considerable difficulties, with regard to singling out the influence of microwaves from the many other factors that are also present. Moreover, such studies require refinement of methods of examining the environment and involvement of specialists in allied fields.

In summary, it should be indicated that, at the present time, Soviet specialists are developing different directions of the problem of microwave radiation as a biologically and hygienically important factor. Attention is concentrated chiefly on the study of biological effects of low-level microwaves, the mechanisms thereof and assessment of the significance of reactions to the organism. Analysis of existing data on correlations between biological effects of microwave radiation and intensity of this factor, duration and mode of exposure made it possible to recommend the maximum permissible levels of this factor for populated areas.

At the present time, it is also possible to formulate a number of problems related to the patterns of microwave effects. To solve these problems, it is imperative to activate scientific research in the relevant direction and to coordinate the work that is being done in order to assure that the methodological approaches are the same and that comparable and mutually supplementary data are obtained.

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CYTOGENETIC AND GONADOTOXIC EFFECTS OF STATIC ELECTRIC FIELDS

Moscow GIGIYENA I SANITARIYA in Russian No 10, Oct 81 (manuscript received 3 Mar 81) pp 9-11

[Article by K. I. Stankevich, L. N. Badayeva, L. V. Samosh and L. Z. Shumova, All-Union Scientific Research Institute of Hygiene and Toxicology of Pesticides, Polymers and Plastics, USSR Ministry of Health, Kiev]

[Text] A static electric field (SEF) is formed on all dielectrics, including synthetic materials used in construction, ship building, aviation, clothing and shoe manufacture, etc. Build-up of SEF on polymers is significantly greater than the natural background. Constant exposure of man to SEF elicits a wide range of changes in different systems, for which reason special studies were pursued (K. I. Stankevich et al.) to set the hygienic SEF at 150 V/cm.

There are reports (A. P. Dubov et al.) of genetic effects of SEF on onion roots. F. G. Portnov et al. discovered that SEF have mutagenic effects on female drosophila. There are no data in the literature concerning the gonadotoxic effects of SEF.

Our objective here was to test the effects of SEF on morphological and genetic structures of testicular cells of white mongrel mice. We evaluated the effects according to incidence of cytogenetic disturbances in meiotic chromosomes at the diakinesis-metaphase I stage in male mice; preparations of testes were submitted to histological analysis. Experiments were conducted on a device that we developed, which consists of a chamber for experimental animals, double-plated electrodes, adjustable brackets, "aerofranklinizer" connected into the power line and a kilovoltmeter.

Field intensity in the chambers was regulated with the aerofranklinizer switch and distance between electrodes, on the basis of $E = V/H$, where E is field intensity, V is voltage on the kilovoltmeter scale and H is distance between electrodes.

We used five groups of mice in the experiments (3 experimental and 2 control), with six animals in each. The tests were conducted in two sessions and in different seasons (summer-fall and winter-spring), so that each had its own control. Moreover, when working with mongrel animals it is assumed that

there is a control for each group of animals. The experimental animals were exposed to SEF of 700 and 300 V/cm (in the summer-fall season), 150 V/cm (in the winter-spring), for 6 h daily for 2 months. The experimental animals were sacrificed 24 h after the last exposure to SEF by dislocating the vertebrae, and preparations of meiotic chromosomes were made from the testes by the method of Evans et al. We submitted 500 cells from each experimental and control group to cytogenetic analysis.

Table 1. Incidence of chromosomal aberrations in the diakinesis-metaphase I after exposing mice to SEF in chronic experiment ($M \pm m$)

Variant	Number of animals	Exposure months	Number of cells examined	Number of diakinesis-metaphases							
				with translocations		with fragments		with autosomal univalents		with X-Y sex univalents	
				abs.	%	abs.	%	abs.	%	abs.	%
Summer-fall											
SEF 700 V/cm	6	2	500	11	$2,5 \pm 0,09$	—	0	5	$1,0 \pm 0,3$	10	$2,0 \pm 0.6$
P					$<0,05$				$>0,05$		$<0,05$
SEF 300 V/cm	6	2	500	1	$0,2 \pm 0,03$	—	0	2	$0,4 \pm 0,2$	5	$1,0 \pm 0,3$
P					$<0,05$				$>0,05$		$<0,05$
Control	6	2	500	—	0	—	0	2	$0.4 \pm 0,2$	1	$0,2 \pm 0.03$
Winter-spring											
SEF 150 V/cm	6	2	500	—	0	3	$0,6 \pm 0,08$	12	$2,4 \pm 0,6$	5	$1,0 \pm 0,3$
P							$>0,05$		$>0,05$		$>0,05$
Control	6	2	500	—	0	5	$1,0 \pm 0,3$	5	$1,0 \pm 0,3$	8	$1,6 \pm 0,5$

The results of this analysis are listed in Table 1, which shows that only autosomal and sex univalents (0.4 and 0.2%, respectively) were encountered in the first control group of mice; no translocations or fragments were demonstrated. Injuries to meiotic chromosomes at the diakinesis-metaphase I stage developed in testicular cells of experimental mice after exposure to 700 V/cm. There was a high incidence of cells with translocations (average 2.5%, versus 0 in the control). Cells with autosomal univalents constituted 1% and with sex univalents 2%, which was considerably above control figures. Chromosomal aberrations appeared under the effect of SEF of 300 V/cm, but there were considerably fewer: the incidence of cells with translocations dropped to 0.2% (there being none in the control). There was also a decrease in cells with sex univalents (1%). The incidence of cells with autosomal univalents was on the control level (0.4%). Such aberrations as fragments were not demonstrated with exposure to 700 and 300 V/cm. No reliable changes were found in mice exposed to SEF of 150 V/cm.

Thus, the results of these tests revealed that SEF of 700 V/cm has a marked cytogenetic effect on the chromosomal system of mouse testicular cells, which is indicative of its potential genetic hazard to sex cells of warm-blooded animals. We established that the effect is a function of dosage: at 700 V/cm there was a statistically significant cytogenetic effect according to the

test for chromosomal aberrations; at 300 V/cm there was a less marked effect and at 150 V/cm we failed to observe reliable differences in any of the parameters.

Table 2. Morphological changes in mouse testes after 2-month exposure to SEF of 150, 300 and 700 V/cm (M±m)

Variant	Exposure time, months	Spermatogenesis index	Total spermatogonia	Number of tubules: with desquamated epithel.	Number of tubules: with 12th meiotic stage
			Summer-fall		
SEF 700 V/cm	2	3,04±0,018	64,5±0,8	2,5±0,7	11,6±0,85
P		<0,05	<0,05	<0,05	<0,05
SEF 150 V/cm	2	3,14±0,25	65,1±2,08	5,4±0,7	12,4±1,5
P		0,05	>0,05	>0,05	<0,05
Control	2	3,24±0,03	56,4±2,8	7,6±0,7	7,4±0,7
			Winter-spring		
SEF 300 V/cm	2	3,08±0,007	53,6±1,1	0,3±0,1	3,0±0,48
P		<0,05	>0,05	<0,05	<0,05
Control	2	2,95±0,02	52,0±0,5	1,5±0,4	1,16±0,1

We studied the gonadotoxic effect of SEF on 5 groups of animals (3 experimental and 2 control), with 10 mice in each group. We assessed the condition of spermatogenic epithelium according to the following parameters: spermatogenesis index (estimated on a 4-point scale in 100 seminiferous tubules), total number of normal spermatogonia (considering all types thereof up to the stage of dormant spermatocytes) and number of degenerative forms (counted in 20 round tubules), number of tubules with desquamated spermatogenic epithelium (counted by examining 100 tubules), number of tubules with 12th stage of meiosis-metaphase II of maturation division (counted in 100 tubules).

We examined 1500 tubules and counted 8533 spermatogonia to determine the second indicator of the gonadotoxic effect. The studies revealed that SEF has a gonadotoxic effect, which is distinct at 700 V/cm (Table 2).

It is apparent from the above data that SEF of 700 V/cm has an adverse effect on the spermatogenic epithelium, causing decline of the spermatogenesis index (3.04±0.018), as compared to the control (3.24±0.03). We estimated the spermatogenesis index on the 4-point scale of Fogg, which considers the presence of four types of spermatogenic epithelial cells in the seminiferous tubules (spermatogonia, spermatocytes, spermatids and spermatozoa). The decline of the index is indicative of impaired spermatogenesis, which is morphologically manifested by a decrease in number of tubules containing all types of spermatogenic epithelial cells.

The increase in total spermatogonia (64.5±0.8, versus 65.4±2.8 in the control) and tubules with the 12th meiotic stage (11.6±0.85, versus 7.4±0.7 in the control) observed under the effect of SEF of 700 V/cm is indicative of the activating effect of SEF on the early stages of formation of spermatogenic epithelium (spermatogonia and spermatocytes). A comparison of these parameters to the decline of spermatogenesis index suggests that SEF of this intensity has an adverse effect on the final stages of formation of spermatogenic epithelial cells, in particular, on formation of spermatids and spermatozoa.

SEF of 300 and 150 V/cm has no adverse effect on the final stages of formation of cells of the spermatogenic epithelium (spermatogenesis index is 3.08±0.007 at 300 V/cm, versus 2.95±0.02 in the control; it is 3.14±0.25 at 150 V/cm, versus 3.24±0.03 in the control). The morphological findings on the effects of SEF on the gonads conform with the cytogenetic data, as well as results of studying its general toxic effect (according to biological parameters).

On the basis of the above data, the threshold and subthreshold indicators of cytogenetic and gonadotoxic effects of SEF are at almost the same level, 300 and 150 V/cm, respectively. At 700 V/cm, SEF had a gonadotoxic and cytogenetic effect under our experimental conditions.

Conclusions

1. SEF has a cytogenetic and gonadotoxic effect on mice.

2. The threshold and subthreshold parameters of cytogenetic and gonadotoxic effects of SEF are on the same level--300 and 150 V/cm, respectively. SEF of 700 V/cm elicits marked changes.

3. Threshold and subthreshold indicators of the cytogenetic and gonadotoxic effects of SEF conform to the levels of its biological effects, where the threshold voltage is 300 V/cm and the subthreshold level is 150 V/cm.

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EFFECTS OF SUPERHIGH FREQUENCY ELECTROMAGNETIC FIELDS ON ANIMALS OF DIFFERENT AGES

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[Article by O. I. Shutenko (deceased), I. P. Kozyarin and I.I. Shvayko, Kiev Medical Institute imeni Academician A. A. Bogomolets]

[Text] Our objective here was to test the effects of superhigh frequency (SHF) electromagnetic fields (EMF) on young (growing) and mature animals. The experimental model consisted of 90 male white rats initially weighing 70-80 and 160-200 g, which were divided into 6 groups of 15 animals in each, depending on intensity of the factor used. The animals of the first (young) and fourth (puberal) groups served as a control. The second, third (young) and fifth, sixth (mature) groups were exposed to an SHF field with energy flux density (EFD) of 10 and 100 $\mu W/cm^2$, respectively, for 2 h/day over a period of 10 weeks. We used the Luch-58 magnetron SHF generator, at working frequency of 2375±50 MHz (wavelength 12.6 cm) as the source of SHF radiation.

The animals were irradiated in groups in the zone of the formed field in an ordinary room with cinder block walls (temperature 18-20°C, humidity 40-60%). We used a PO-1 instrument (Medik-1) for dosimetry. We measured EFD of the SHF field over the entire area of the room. The animal cages were placed in areas where the fields constituted 10 and 100 $\mu W/cm^2$.

To assess the effects of SHF energy, we examined the following parameters: integral (dynamics of body weight, duration of hexenal sleep, work capacity--swimming with a weight equaling 10% of body weight), functional state of the central nervous system (summation-threshold index--STI, latency period of unconditioned reflex), some biochemical parameters (cholinesterase activity of blood and brain tissue, glycogen content of hepatic tissue, ascorbic acid in adrenal and liver tissue, lactic acid in blood, activity of succinate and α-ketoglutarate dehydrogenases of liver mitochondria, supravital stain of brain and liver tissue), coefficients of visceral mass, morphological composition of peripheral blood, as well as balance and interorganic distribution of trace elements (copper, molybdenum, iron and manganese).

We submitted the results to statistical processing, with calculation of Student-Fisher criteria, considering differences reliable with $P<0.05$. Summarized results are listed in Tables 1 and 2, in which reliable differences in parameters of control and experimental animals are marked with an asterisk.

Table 1. Functional state of animals by the end of the experiment with exposure to SHF energy (M±m)

Parameter	Young animals			Mature animals		
	1st group (control)	2d group (10 μW/cm^2)	3d group (100 μW/cm^2)	4th group (control)	5th group (10 μW/cm^2)	6th group (100 μW/cm^2)
Body weight, g	147,6±12,3	147,5±14,0	141,0±13,5	298,0±30,2	297,7±30,1	292,7±28,1
Swimming test, s	125,0±8,1	114,0±10,9	113,0±10,5	263,0±7,8	231,0±13,0	239,0±34,8
Duration of drug-induced sleep, min	12,5±1,1	18,0±3,0	11,3±1,8	19,0±3,0	15,7±0,8	18,9±3,0
STI, V	10,8±0,4	11,1±0,5	12,3±0,4*	13,0±0,6	14,2±0,5	14,8±0,4*
Unconditioned reflex latency period, ms	42,9±1,6	50,0±1,3*	53,6±1,6*	53,8±1,7	48,8±2,1	59,1±2,8
Blood cholinesterase activity, mM/(mℓ•h)	39,1±1,9	32,0±3,0	23,9±1,7*	41,2±2,1	33,7±4,0	32,4±4,7
Brain cholinesterase activ., mM/(g•h)	854±25,0	692,0±28,0*	476,0±48,0*	761,0±56,0	556,0±40,0*	518,0±50,0*
Vitamin C of adrenal tissue, mg%	321,0±9,9	376,0±8,5*	369,0±3,9*	344,4±14,3	382,0±21,6	350,0±24,0
SDH activity of liver mitochondria, μg formasan/g protein	3,75±0,28	3,66±0,29	3,08±0,13*	3,33±0,32	3,26±0,35	3,64±0,26
Eosinophils/μg blood	61,0±6,0	89,0±6,0*	93,0±11,0*	57,0±5,0	69,0±9,0	78,0±9,0*
Activity of α-ketoglutarate dehydrogenase of liver mitochondria, μg ferrocyanide/g protein	74,1±9,8	68,3±7,7	80,8±7,4	79,2±10,1	74,2±4,3	80,0±5,7

*P<0.05

Analysis of our findings revealed that there were no changes in weight of intact and experimental animals in the course of the experiment (see Table 1). Nor was there any difference from the control in work capacity and duration of hexenal sleep in irradiated animals. The most marked and reliable changes were referable to parameters of functional state of the central nervous system, which were characterized by inhibitory processes: longer reflex latency period and increased STI. A longer latency period was observed in young animals (2d and 3d groups) at the end of the experiment, whereas it did not differ from the control in mature ones (5th and 6th groups). The STI changes in young animals were characterized by a reliable increase after 4 experimental weeks, with subsequent normalization by the end of the experiment (2d group) and significant increase ($P<0.05$) during the entire exposure period in the 3d group (EFD 100 $\mu W/cm^2$). Among the mature animals, an increase in STI was recorded only for the 6th group (EFD 100 $\mu W/cm^2$) 10 weeks after the start of the experiment (see Table 1). Evidently, the demonstrated changes in the central nervous system are protective in nature, and they are related to the organism's defense-compensatory reaction to SHF energy.

Table 2. Levels of trace elements (in mg%) in animal tissues at the end of the experiment with exposure to SHF energy (M±m)

Specimen examined	Young animals			Mature animals		
	1st group (control)	2d group (10 $\mu W/cm^2$)	3d group (100 $\mu W/cm^2$)	4th group (control)	5th group (10 $\mu W/cm^2$)	6th group (100 $\mu W/cm^2$)
			Copper			
Liver	661,3±58,7	512,9±50,0	312,5±29,4**	466,2±46,0	432,4±42,0	359,1±35,0**
Brain	128,4±11,6	189,3±17,4*	290,5±18,0**	119,2±10,1	140,5±14,0	217,8±21,5**
Myocardium	118,5±11,0	125,4±12,1	212,3±20,9**	98,3±9,0	112,7±11,0	184,5±17,7**
Blood	63,1±6,6	56,2±5,4	47,4±4,5	44,8±4,2	58,2±5,5	81,2±8,0
			Molybdenum			
Liver	52,7±5,1	38,4±3,7	27,3±2,8**	49,0±5,0	41,4±0,4	38,4±4,0
Brain	8,9±0,7	4,6±0,5	3,9±0,4**	6,2±0,6	5,1±0,5	4,3±0,4*
Myocardium	3,8±0,4	3,1±0,3	2,1±0,2*	3,2±0,3	3,2±0,3	2,4±0,2
Blood	3,1±0,3	4,2±0,4	5,3±0,5*	2,5±0,2	2,5±0,2	2,1±0,2
			Iron			
Liver	27,4±2,8	31,2±3,0	46,5±4,5*	18,1±2,0	24,7±2,5	38,5±3,9**
Brain	14,3±1,2	9,3±0,8**	5,7±0,6**	9,3±0,9	7,8±0,8	4,2±0,4**
Myocardium	5,4±0,5	10,2±1,0**	12,3±1,2**	6,9±0,7	7,4±0,7	9,1±0,8*
Blood	42,7±4,7	33,2±3,1	25,3±2,4**	33,2±3,2	25,1±2,5	19,2±2,0**
			Manganese			
Liver	169,6±15,8	203,4±20,0	319,5±30,5**	132,3±12,8	171,4±17,2	215,5±20,5*
Brain	19,5±1,8	17,2±1,6	16,7±1,5	21,8±2,0	21,8±1,9	28,4±2,7
Myocardium	22,6±2,0	19,5±2,0	13,8±1,4**	17,6±1,8	17,6±1,8	21,3±2,1
Blood	5,4±0,5	3,2±0,3	2,4±0,2**	3,4±0,3	4,6±0,5	5,7±0,6*

* $P<0{,}05$.
** $P<0{,}01$.

The enzyme, cholinesterase, plays an important role in implementing specific functional activity of the nervous system, and we devoted special attention to it. Table 1 shows that the level thereof declined toward the end of the experiment in blood (reliably in the 3d group of animals) and brain tissue (2d, 3d and 5th, 6th). Evidently the decrease in blood cholinesterase activity should be interpreted as an adverse sign, which could be the cause of impaired nervous system function due to change in correlation between excitatory and inhibitory processes, as well as impairment of neurohumoral regulation (D. Ye. Al'pern).

Impairment of secretory function of the adrenal cortex is associated with change in ascorbic acid concentration of the adrenals (N. P. Zalyubovskaya). As we see in Table 1, exposure to SHF energy elicits an increase in ascorbic acid content of the adrenals of young animals (2d and 3d groups), with no change in mature ones. The demonstrated changes in ascorbic acid content of the adrenals of young animals apparently reflect, to some extent, functional changes in the central elements of the hypothalamus--hypophysis--adrenal system.

A comparison of the weight of the liver, kidneys, adrenals, brain, heart and spleen of irradiated and nonirradiated animals failed to demonstrate significant differences.

The blood changes are particularly sensitive reactions of the organism to radiowaves of different ranges. In view of this, we determined the quantity of leukocytes, erythrocytes and eosinophils of peripheral blood 10 weeks after the start of exposure.

The results of these studies revealed that there is relative increase under the influence of the SHF field of eosinophil content of the blood of young (2d and 3d groups) and mature (6th group) animals, and this is perhaps related to functional impairment of endocrine glands, in particular, the adrenal cortex (O. I. Shutenko).

Studies of succinate and α-ketoglutarate dehydrogenase activity revealed a statistically significant ($P<0.05$) decrease in SHD activity only in young animals after 10 weeks of exposure to an SHF field with intensity of 100 $\mu W/cm^2$ (3d group). SDH is referable to the group of oxidative enzymes that catalyze the process of dehydration of succinic acid. A decrease in its activity could lead to distortion of reactions that occur under normal conditions at a different intensity (N. T. Raykhlin). The changes in SHD activity that we demonstrated are consistent with the data of other researchers (V. G. Lazarovich; R. D. Gabovich et al., and others).

Evidently, the changes in activity of oxidative enzymes are related to redistribution of trace elements in response to radiowaves, and the results of examining them are listed in Table 2. We cannot rule out the possibility that the decrease in SDH activity is due to decline of copper level in the liver of young animals and elevation of iron level, since these metals are contained in respiratory enzymes and are electron carriers in the respiratory chain (A. O. Voynar).

There were the following changes in metabolism and redistribution of copper and iron in other organs and tissues: reliable increase in iron content of the kidneys, lungs, myocardium and decrease in the spleen, brain, skeletal muscles, bones, skin and blood of young and mature animals (impairment of Fe homeostasis). Under the influence of SHF energy, there was an increase in copper content of the lungs, brain, myocardium, skeletal muscles, blood (6th group of animals) and decrease in the kidneys (see Table 2). The changes in molybdenum metabolism in organs and tissues were in different directions, with the exception of the liver. There was distinctive change in manganese metabolism with exposure to SHF: elevation in the liver, spleen, skin, kidneys of young and old animals and reliable drop in the myocardium and bones of rats in the 3d group. Blood manganese content was diminished ($P<0.01$) in young animals (3d group) and increased in mature ones (6th group), i.e., there was impairment of Mn homeostasis.

Thus, the disturbances referable to metabolism and redistribution of copper, molybdenum, iron and manganese were more marked in young animals that mature ones, and they were directly related to the intensity of the factor under study.

Conclusions

1. Young animals are more sensitive to SHF radiation than mature ones.

2. In developing scientifically validated maximum permissible levels of physical environmental factors, one must also take into consideration the age factor (increase protection of children's institutions in the range of the factor by widening health-protection zones or by fortifying shielding fencing, etc.).

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